

SYSTEMIC PATHOLOGY



Ali EL-Hindawi

2010 - 2011

VISIT...

LANZAROTE
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DEDICATION

To the soul of my parents
To my beloved family
To my students

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PREFACE

Endless thanks for the almighty of Allah, our great God who gave me power, spirit and perseverance during re-writing of this book.

In this new edition of "Systemic Pathology" many of the topics were rewritten and updated. I hope that this book will meet the essential demands of the medical students in understanding the pathology of the different diseases affecting the body systems.

Prof. Ali El Hindawi
September 2010

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DISEASES OF THE HEART

RHEUMATIC FEVER

AETIOLOGY AND PATHOGENESIS

DEFINITION:

Rheumatic fever is an autoimmune collagen disease affecting the heart & extracardiac sites.

INCIDENCE:

Much lower in developed countries than in poor communities. This is because rheumatic fever is predisposed to by upper respiratory tract streptococcal infection which is more common in low socioeconomic people who are more susceptible to infections due to crowding, bad housing...etc. The disease is common in Egypt.

AGE:

The disease affects children and young adults between the ages of 5-15 years.

AETIOLOGY & PATHOGENESIS:

The disease starts as upper respiratory infection (pharyngitis, tonsillitis...) with group A beta hemolytic Streptococci (rheumatogenic streptococci). Then after a latent period of 2-5 weeks rheumatic lesions develop. However, bacteria are neither detected in the rheumatic lesions nor in the blood, suggesting an autoimmune disease mediated by one of the following mechanisms:

a-Antigenic Similarity (cross-reactivity): Antibodies against streptococcal antigen (M protein) cross react with human tissue antigens, mainly connective tissue glycoproteins and sarcolemma of muscle, since they are immunologically identical. Numerous antistreptococcal antibodies are produced e.g. antistreptolysin O (ASO).

b-Altered antigenicity: Binding of streptococcal antigen to human tissue may render it antigenic → antibodies against these human tissues (autoantibodies), including antibodies against collagen and myocardium.

It has to be noted that, not all people subjected to upper respiratory infection with group A beta hemolytic Streptococci develop rheumatic fever. Some people have a greater genetic predisposition towards an abnormal immune response and young ages are the main susceptibles.

CLINICAL COURSE OF RHEUMATIC FEVER

PHASES OF RHEUMATIC FEVER:

1-Acute phase: It involves the heart and extracardiac sites (joints, brain, skin and others).

2-Chronic phase:

- It involves the heart only. All extracardiac lesions resolve completely without chronicity.
- The chronic rheumatic heart disease is manifested by fibrosis; which most significantly affects the cardiac valves. Clinical manifestations of the chronic phase do not usually appear before at least 10 years & sometimes several decades. Recurrent attacks of rheumatic heart disease due to recurrent upper respiratory tract infections with the rheumatogenic streptococci, lead to more cardiac damage.

COMPLICATIONS OF RHEUMATIC FEVER:

1-Subacute infective endocarditis.

2-Heart failure: It is mainly due to valve lesions (stenosis, incompetence or both). Severe rheumatic myocarditis and pericardial adhesions may contribute.

CHAPTER I

V.I.P + Jar + Gase
No slide

3 organisms
= 3 Bacteria
① R. fever
② subacute infective
③ acute infective

* Autoimmune bec
bacteria not found in blood
not found in lesions

فتر مريض

* الحصى الرئوية
* التهاب الرئة
* التهاب الكبد
* التهاب البنكرياس
* التهاب القولون
* التهاب المثانة
* التهاب البروستاتا

* أمراض
قتل
التهاب
التهاب
التهاب

Antigenic
Altered
Antigenicity

بعض الناس
يولدوا
بمرض

acute
chronic
only

Subacute infective
endocarditis
Heart failure

Myocarditis

* acute + chronic
* extra
* acute only

* Diseases of usually on left side due to pressure

PATHOLOGY OF RHEUMATIC FEVER

Lesions appear within the stroma of heart or extracardiac sites:

1-RHEUMATIC HEART DISEASE (RHD)

All heart layers are affected (pancarditis):

a) **RHEUMATIC MYOCARDITIS:** It mainly affects the myocardium of left side of heart.

Acute Phase: It is characterized by the development of pathognomonic lesions called Aschoff bodies within the interstitium of the myocardium. The condition may rarely be severe → fulminant myocarditis → acute heart failure and death.

Gross Features: Aschoff bodies are multiple tiny grayish nodules, each about 1-2 mm-in diameter & are therefore hardly seen by the naked eye.

Microscopic Features: Each Aschoff body is a paravascular lesion composed of a center of fibrinoid necrosis (destroyed fragmented collagen), surrounded by lymphocytes, histiocytes & Aschoff cells (which are large mononuclear or multinucleated cells of histiocytic origin). The cardiac muscle near the Aschoff bodies shows oedema and slight inflammation. Fibrosis does not develop except after years (see chronic phase).

Chronic Phase: Over years or decades the Aschoff bodies undergo fibrous scarring.

b) **RHEUMATIC PERICARDITIS:** dry serofibrinous inflammation

Acute phase: The visceral and parietal layers of the pericardium show serofibrinous inflammation, usually of the dry type. Fibrin deposited between the visceral and parietal layers gives the pericardium a "bread and butter" appearance.

Chronic Phase: Fibrosis develops and may take the form of "milk spots".
- Whitish patches on the surface, sometimes referred to as "milk spots".
- Adhesions between the visceral and parietal layers of the pericardium.
- Adhesions between the parietal layer of pericardium & mediastinal structures (adherent mediastino-pericarditis).

c) **RHEUMATIC ENDOCARDITIS:** It affects both mural and valvular endocardium:

Mural Endocardium: Left sided endocardium is more commonly affected.

Acute phase: Several Aschoff bodies develop, particularly in the mural endocardium lining the posterior wall of left atrium.

Chronic phase: Healing results in a white patch at the posterior wall of left atrium called "Mac Callum's patch".

Valvular Endocardium: Left sided valves (mitral & aortic) are more commonly affected (mitral alone: 75%, mitral & aortic: 25%). Tricuspid and pulmonary valves may be also affected.

Acute phase:

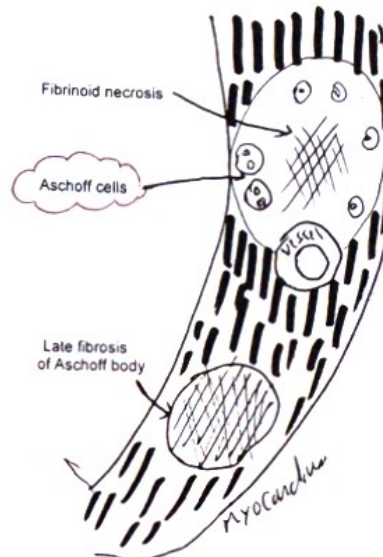
Valve cusps are swollen due to inflammation (lymphocytes and histiocytes) and oedema. **Vegetations** (thrombi) develop. They occur at the lines of contact of the cusps due to endothelial damage at these sites caused by friction of the swollen cusps. Therefore these vegetations are best seen on the atrial surface of the mitral and tricuspid valves and on the ventricular surface of the aortic and pulmonary valves. They appear as multiple small (1-3 mm each), grayish lesions, firmly adherent to cusps.

Chronic phase (chronic rheumatic valvulitis):

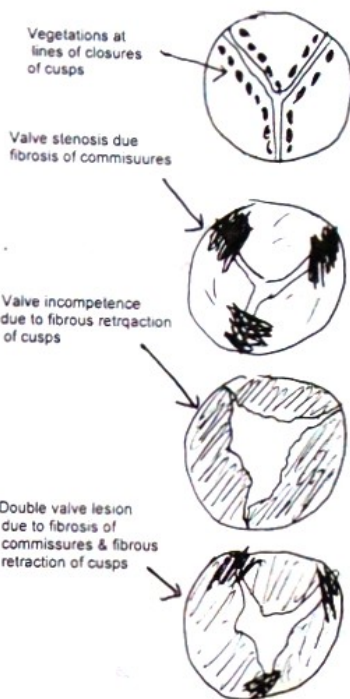
Fibrosis of the inflamed cusps (with fibrous organization of the vegetations) develops & may be minimal or marked. Marked fibrosis leads to valve lesions, which may be:

- **Valve stenosis** due to bridging fibrosis across the commissures.
- **Valve incompetence** due to retraction of the fibrotic cusps.
- **Double valve lesion** (both stenosis and incompetence).

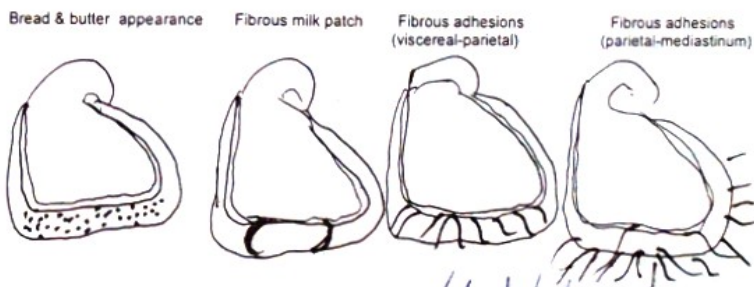
RHEUMATIC MYOCARDITIS (Aschoff Nodule)



RHEUMATIC ENDOCARDITIS



RHEUMATIC PERICARDITIS



White ring-like zone

is more blessed to give than to receive

Vegetations = small thrombi

@ Jaka Sami = ↑ blood supply = ↑ antibody

2- EXTRACARDIAC LESIONS OF RHEUMATIC FEVER:

- Rheumatic arthritis** affects the large joints in a fleeting way i.e. joint inflammation is followed by joint resolution, then another joint becomes inflamed followed by resolution and so on. The affected joint is painful, tender, red, hot & swollen. Microscopically it shows congestion, oedema, lymphocytes, plasma cells and macrophages.
- Brain:** Rheumatic chorea (rapid involuntary purposeless movements). It is due to inflammation of the basal ganglia. The condition is reversible.
- Skin:** Rheumatic subcutaneous nodules may occur over bony prominences. They are 2-20 mm in diameter. Their microscopic structure is similar to Aschoff bodies.
- Pleurisy and Peritonitis** (serofibrinous) may occur.
- Rheumatic pneumonitis** may also occur.
- Rheumatic arteritis** (hypersensitivity angitis) may affect coronary, renal, mesenteric and cerebral arteries as well as aorta and pulmonary arteries.

ENDOCARDITIS

DEFINITION:

Inflammation of the valvular endocardium, with or without the mural endocardium.

TYPES: Endocarditis may be classified into:

1- Infective Endocarditis

- a) Acute infective endocarditis.
- b) Subacute infective endocarditis.

2- Non-infective Endocarditis:

- a) Rheumatic endocarditis
- b) Verrucous endocarditis (Libman-Sacks endocarditis) in case of systemic lupus erythematosus (SLE)
- c) Nonbacterial thrombotic endocarditis: It occurs in prolonged debilitating illness as cancer & uremia. Sterile vegetations occur & may → embolism

ACUTE INFECTIVE ENDOCARDITIS

SUBACUTE INFECTIVE ENDOCARDITIS

AETIOLOGY & PATHOGENESIS

- This is acute suppurative inflammation that can affect healthy valves.
- The causative organisms are highly virulent as Staph. aureus, Strept. hemolyticus, gonococci... These virulent organisms reach the blood (septicemia) in case of severe infections as puerperal sepsis, gonorrhea, intravenous drug abusers...etc.

- This is subacute inflammation that affects predisposed valves as:
 - 1- Rheumatic valvulitis.
 - 2- Congenital anomalies as bicuspid aortic valve.
 - 3- Prosthetic valves.
- The causative organisms are less virulent & cannot invade healthy valves. In predisposed valves, micro-vegetations may exist which become invaded by the bacteria. Streptococcus viridans are the most common organisms (95%) they are normal commensals of throat. They may reach the blood (bacteremia) after tooth extraction or tonsillectomy.

PATHOLOGY AND COMPLICATIONS

1- Valve Lesions

Mitral and aortic valves are the most commonly affected valves. Tricuspid valve is the main affected valve in case of intravenous drug abusers (addicts). The mural endocardium may be also affected. The affected valves (and mural endocardium) show:

- Acute suppurative inflammation → perforation of the affected valve cusps.
- Vegetations:

Mitral and aortic valves are the most commonly affected valves. The mural endocardium may be also affected e.g. MacCallum's patch and the mural endocardium of the right ventricle opposite a ventricular septal defect. The affected valves (and mural endocardium) show:

- Pathology of the original predisposing disease (rheumatic or congenital).
- Vegetations:

Aetiology & Causative organism
Mode of Trans.
Predisposing factor

Gross: Multiple, bulky, yellowish gray friable (detachable) vegetations developing anywhere on the cusps. Microscopic: The vegetations consist of platelets, fibrin, bacteria, neutrophils & pus cells.	Gross: Multiple, large, grayish, friable (detachable) vegetations developing anywhere on the cusps (and sometimes on MacCallum's patch) Microscopic: Vegetations consist of platelets, fibrin, bacteria & some inflammatory cells mainly histiocytes.
--	--

2- Myocardial Lesions:

Severe myocardial degenerative changes	Myocardial degenerative changes.
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3- Embolic Lesions:

Detachment of the septic vegetations → systemic pyemia.	The detached emboli contain low virulent bacteria that do not cause pyemia. These emboli lead to: - Infarction of kidney, brain, spleen... etc. - Embolization of retinal artery (leading to blindness) - Coronary embolism (rare). - Mycotic aneurysms: - The impacted embolus → mild inflammation of the vascular wall → fibrosis (weakening) → dilatation under the effect of the arterial pressure → aneurysm. - These inflammatory (mycotic) aneurysms are most common in cerebral & mesenteric arteries. - Osler's nodules: small tender nodules in pulps of fingers & toes. - Focal embolic glomerulonephritis (see below).
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4- Toxic Lesions:

Severe toxemia, as a part of septicemia (see general pathology for toxemia & septicemia)	- Moderate toxemia causing - Fever, anemia, clubbing of fingers, - Splenomegaly, liver and renal degenerations. - Petechial hemorrhages - Focal glomerulonephritis: - Mechanism: Formerly thought to be due to emboli & was termed focal embolic glomerulonephritis. Now believed to be due to hypersensitivity induced by bacterial antigens → allergic capillaritis. - Microscopy: Focal glomerular necrosis & inflammation. - Grossly the kidney shows petechial hemorrhages (flea-bitten kidney). - Clinically hematuria and finally renal failure.
--	--

COURSE & PROGNOSIS OF INFECTIVE ENDOCARDITIS

Rapidly fatal due to: a) Severe toxemia (septicemia) b) Cusp perforation (incompetence).	a) Can be treated, and the patient survives longer than in acute infective endocarditis. b) Healing of the valves (fibrosis) leads to valve stenosis or incompetence → heart failure.
--	--

no embolism ← adherent
detachable
Rheumatic is smallest vegetations
Acute infective endocarditis largest bulky
Subacute infective endocarditis large veg.

Rheumatic fever
echo shows white vegetations on Mitral valve

ACUTE INFECTIVE ENDOCARDITIS**Vegetations:**

- Any where
- Bulky
- Detachable
- Septic

Associated with perforation

VALVE LESIONS**Vegetations:**

- Any where
- Bulky
- Detachable
- Aseptic (low virulence)

No perforation



Rheumatic endocarditis for comparison

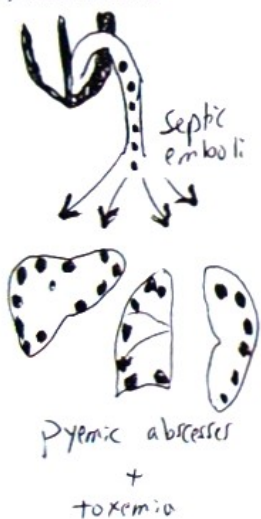
Vegetations

- At lines of closure
- Small
- Adherent
- Aseptic

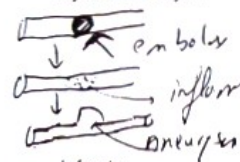
No perforation

**EMBOLIC & TOXIC LESIONS**

Pyemia & Toxaemia



Mycotic aneurysm



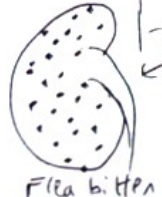
Infarcts



Osler's nodules

Finger clubbing
Focal glomerulonephritis

Splénomegaly



Flea bitten

Aetiology: ① Congenital
 ② Rheumatic
 ③ Healed subacute infective endocarditis
 Incompetence → ④ acute infective endocarditis ⑤ functional Incompetence
 MCQ + JE

DISEASES OF VALVES**MITRAL STENOSIS****AETIOLOGY:**

- 1- Rheumatic (chronic rheumatic valvulitis)
- 2- Healed subacute infective endocarditis.

PATHOLOGY:

- 1- Mitral cusps are thickened, irregular and fused.
- 2- Mitral orifice is narrowed and may appear slit-like (button hole shaped).
- 3- Mitral valve appears funnel-shaped when seen from the atrial side.
- 4- Cordae tendinae are fibrosed and shortened.
- 5- Papillary muscles are hypertrophied

EFFECTS AND COMPLICATIONS:

- 1- Left ventricle is not hypertrophied
- 2- Left atrium:
 - a) Hypertrophy and dilatation.
 - b) Thrombosis may occur.
- 3- Lung congestion (see general pathology).
- 4- Pulmonary hypertension occurs later.
- 5- Right ventricular hypertrophy, dilatation and failure
- 6- Right atrium
 - a) Hypertrophy and dilatation
 - b) Thrombosis may occur.
- 7- Chronic general venous congestion due to right ventricular failure (see general pathology).
- 8- Lung infarcts are common due to:
 - a) Low cardiac output leading to inefficient bronchial blood flow
 - b) Pulmonary embolism is common due to fragmentation of right atrial thrombus or derived from a leg vein thrombus which is common in cases of right sided heart failure.
- 9- Subacute infective endocarditis may complicate mitral stenosis (or any other valve disease)

MITRAL INCOMPETENCE**AETIOLOGY:**

- 1- Rheumatic.
- 2- Healed subacute infective endocarditis.
- 3- Acute infective endocarditis (damage of cusps).
- 4- Left ventricular dilatation (e.g. due to hypertension). leads to dilatation of mitral ring & incompetence.
- 5- Mitral prolapse (floppy mitral valve syndrome) which is due to idiopathic myxomatous changes of the mitral cusps

EFFECTS AND COMPLICATIONS:

- 1- Left ventricle: Hypertrophy, dilatation and failure. This is because regurgitation of blood into the left atrium during systole will increase ventricular filling during diastole (volume load).
- 2- Left atrium: Hypertrophy, dilatation.
- 3- Lungs: Congested (describe).
- 4- Pulmonary hypertension.
- 5- Right ventricle: Hypertrophy, dilatation and failure
- 6- Right atrium: Hypertrophy, dilatation.
- 7- Chronic general venous congestion

AORTIC STENOSIS**AETIOLOGY:**

- 1- Chronic rheumatic valvulitis.
- 2- Congenital (rare).
- 3- Healed subacute infective endocarditis.
- 4- Atherosclerosis.

Calcified and fused
 case parietal
 reg. of
 no hypertrophy
 left ventricle

ACUTE INFECTIVE ENDOCARDITIS

SUBACUTE INFECTIVE ENDOCARDITIS

VALVE LESIONS

Vegetations:

- Any where
 - Bulky
 - Detachable
 - Septic
- Associated with perforation



Vegetations:

- Any where
 - Bulky
 - Detachable
 - Aseptic (low virulence)
- No perforation



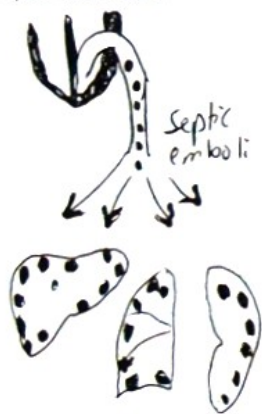
Rheumatic endocarditis for comparison

- At lines of closure
 - Small
 - Adherent
 - Aseptic
- No perforation



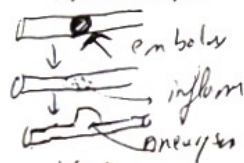
EMBOLIC & TOXIC LESIONS

Pyemia & Toxaemia



Pyemic abscesses
+
toxemia

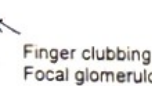
Mycotic aneurysm



Infarcts



Osler's nodules



Finger clubbing

Focal glomerulonephritis

Splenomegaly



Flea bitten



Aetiology: 1. Congenital stenosis 2. Rheumatic 3. Healed subacute infective endocarditis 4. Acute infective endocarditis 5. Functional incompetence MCQ + JE

DISEASES OF VALVES

MITRAL STENOSIS

AETIOLOGY:

- 1- Rheumatic (chronic rheumatic valvulitis)
- 2- Healed subacute infective endocarditis.

PATHOLOGY:

- 1- Mitral cusps are thickened, irregular and fused.
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- 4- Pulmonary hypertension occurs later.
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- 6- Right atrium
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- 2- Healed subacute infective endocarditis.
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EFFECTS AND COMPLICATIONS:

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- 2- Left atrium: Hypertrophy, dilatation.
- 3- Lungs: Congested (describe).
- 4- Pulmonary hypertension.
- 5- Right ventricle: Hypertrophy, dilatation and failure
- 6- Right atrium: Hypertrophy, dilatation.
- 7- Chronic general venous congestion

AORTIC STENOSIS

AETIOLOGY:

- 1- Chronic rheumatic valvulitis.
- 2- Congenital (rare).
- 3- Healed subacute infective endocarditis.
- 4- Atherosclerosis.

Calcification of aortic valve
No hypertrophy of left ventricle

EFFECTS AND COMPLICATIONS:

- 1-Left ventricle: Hypertrophy, dilatation and failure (pressure load).
- 2-Left atrium: Hypertrophy, dilatation.
- 3-Lung congestion.
- 4-Pulmonary hypertension.
- 5-Right ventricular hypertrophy, dilatation and failure.
- 6-Right atrial hypertrophy and dilatation.
- 7-Chronic general venous congestion.
- 8-Decreased coronary flow leading to angina pectoris.

AORTIC INCOMPETENCE A

AETIOLOGY:

- 1-Chronic rheumatic valvulitis.
- 2-Congenital bicuspid aortic valve.
- 3-Atherosclerosis.
- 4-Healed subacute infective endocarditis.
- 5-Acute infective endocarditis.
- 6-Syphilitic aortitis.

EFFECTS AND COMPLICATIONS:

- 1-Left ventricle: Hypertrophy, dilatation & failure due to high volume load caused by regurgitation of blood into the left ventricle during diastole. Dilatation of the left ventricle → relative mitral incompetence → further hypertrophy & dilatation of left ventricle.
- 2-Left atrium: Hypertrophy, dilatation.
- 3-Lung congestion.
- 4-Pulmonary hypertension.
- 5-Right ventricular hypertrophy, dilatation, failure.
- 6-Right atrium: Hypertrophy and dilatation.
- 7-Chronic general venous congestion.
- 8-Marked decrease of coronary flow due to aortic regurgitation leads to angina pectoris.

REMARK: When all cardiac chambers are dilated the condition is known as *cor bovinum*. This is most marked in cases of aortic incompetence.

PULMONARY STENOSIS B

AETIOLOGY:

- 1-Chronic rheumatic valvulitis.
- 2-Healed subacute infective endocarditis.
- 3- Congenital stenosis (most common cause).
- 4-Carcinoid syndrome.

PATHOLOGY:

- 1-Left ventricle and left atrium: Unaffected.
- 2-Lungs: Pale anemic due to decreased pulmonary flow.
- 3-Right side: Hypertrophy, dilatation and failure (chronic general venous congestion).

TRICUSPID INCOMPETENCE B

AETIOLOGY:

- 1-Chronic rheumatic valvulitis.
- 2-Healed subacute infective endocarditis.
- 3- Acute infective endocarditis.
- 4-Relative incompetence occurs in case of right ventricular dilatation, which leads to dilatation of the atrioventricular ring.

PATHOLOGY:

- 1-Left side of heart: Unaffected.
- 2-Lungs: Pale anemic.
- 3-Right side: Hypertrophy, dilatation and failure (chronic general venous congestion).

MITRAL STENOSIS

Narrow orifice

Funnel shaped

Papillary muscle Hypertrophy

Short chordae tendinae

Normal Mitral Valve



Effects of Mitral Stenosis
Congested lungs

Pulmonary hypertension

Left atrial hypertrophy & dilatation

Left ventricle not hypertrophied

Rt. side hypertrophy & dilatation

Thrombi



MITRAL INCOMPETENCE

Hypertrophy & dilatation of all
Chambers (*cor bovinum*)

Lung congestion



Cor bovinum

DISEASES OF MYOCARDIUM

CARDIOMYOPATHY (MCQ) (x)

1) PRIMARY (IDIOPATHIC) CARDIOMYOPATHY:

Definition: This is heart muscle (myocardial) disease of unknown cause.

Types: Three types:

a) Dilated (Congestive) Cardiomyopathy:

- Most common type (90%). It occurs at any age
- Aetiology is unknown, but suspected causes include alcohol, previous viral myocarditis, genetic & nutritional disorders
- The heart is markedly dilated and the contractility is impaired

b) Hypertrophic Cardiomyopathy (Idiopathic Hypertrophic Subaortic Stenosis):

- In more than 50% of cases the disease is familial (autosomal dominant inheritance).
- There is asymmetrical left ventricular hypertrophy particularly septal.

c) Restrictive (obliterative) Cardiomyopathy:

The rarest type.

There is cardiac rigidity → reduction of ventricular diastolic filling → low cardiac output.

2) SECONDARY CARDIOMYOPATHY:

Definition: This is myocardial disease related to specific causes.

Causes:

- Inflammatory: Myocarditis
- Toxic: alcohol
- Thyrotoxicosis
- Amyloidosis
- Sarcoidosis
- Glycogen storage disease
- Congenital: Endocardial fibroelastosis or endomyocardial fibrosis.

Effects:

Variable (according to severity of the condition). Severe forms may include restrictive cardiomyopathy

MYOCARDITIS B(x) قسط في القلب

Definition:

This is myocardial inflammation, usually acute, may resolve or progress to heart failure.

Types of myocarditis:

- 1-Rheumatic myocarditis.
- 2-Viral myocarditis: Caused by Coxsackie B virus (or other viruses). The interstitial tissue of the myocardium shows diffuse infiltration with lymphocytes, plasma cells & macrophages.
- 3-Toxic myocarditis: As in cases of diphtheria.
- 4-Acute interstitial myocarditis (Fiedler's myocarditis): It occurs in young persons and the aetiology is unknown. There is diffuse infiltration of the interstitial tissue of the myocardium with neutrophils, macrophages, lymphocytes and sometimes giant cells.
- 5-Suppurative myocarditis (abscesses) in case of septicemia.
- 6-Tuberculous myocarditis.
- 7-Syphilitic myocarditis.
- 8-Parasitic myocarditis as trichinella spiralis
- 9-Radiation myocarditis

PERICARDIAL DISEASE

PERICARDITIS 2011

SEROFIBRINOUS PERICARDITIS:

Aetiology:

- 1) Rheumatic fever
- 2) Uremia
- 3) Myocardial infarction
- 4) Viral (Coxsackie B virus)
- 5) Bacterial (e. g. as complication of pneumonia).
- 6) Malignant tumors of pericardium (primary or metastatic).

Pathology: See general pathology.

SUPPURATIVE (PURULENT) PERICARDITIS:

Aetiology: Pyogenic bacteria (staphylococci, Streptococci...etc) reach the pericardium through:

- 1) Blood route (in cases of septicemia).
- 2) Direct or lymphatic routes from lung infections as pneumonia, abscess, empyema or from osteomyelitis of a rib.

Pathology: Pus accumulates in the pericardial sac. Toxemia is severe. Surviving patients develop dense pericardial fibrosis resulting in adhesions, constrictive pericarditis or adherent mediastino-pericarditis.

TUBERCULOUS PERICARDITIS:

It is usually due to spread from pulmonary tuberculosis. Dense pericardial fibrosis may occur resulting in adhesions, constrictive pericarditis or adherent mediastino-pericarditis.

ADHERENT MEDIASTINO-PERICARDITIS:

Aetiology: May be due to healing of suppurative or tuberculous pericarditis.

Pathology: The pericardial sac is obliterated with adherence of the external aspect of the parietal layer to the surrounding structures. During systole, the heart pulls not only against the parietal pericardium, but also against the surrounding structures. The increased workload causes cardiac hypertrophy and dilatation, which may be massive.

CONSTRICTIVE PERICARDITIS:

Aetiology: It results from healing of suppurative or tuberculous pericarditis

Pathology: The pericardial sac is obliterated by dense fibrosis adhering the visceral to the parietal layer. The diastolic filling of the heart is reduced (resembling restrictive cardiomyopathy) and the orifices of the venae cava are constricted leading to chronic generalized venous congestion. Cardiac hypertrophy and dilatation do not occur.

MYCOTIC (FUNGAL) PERICARDITIS: Rare. Occurs in disseminated fungal infections.

HYDROPERICARDIUM B(x)

This is accumulation of transudate (serous fluid) in the pericardial sac in cases of generalized oedema (cardiac, renal or nutritional).

HAEMOPERICARDIUM B(x)

Definition: This is accumulation of blood within the pericardial sac.

Aetiology:

- 1) Rupture of recent or healed cardiac infarct, or cardiac aneurysm.
 - 2) Rupture of aortic aneurysm.
 - 3) Others: Trauma, blood diseases as leukemia, pericardial tumors.
- Effects:** 1) Cardiac compression (cardiac tamponade) → acute heart failure 2) Shock.

CORONARY (ISCHEMIC) HEART DISEASE

A) CHRONIC ISCHAEMIA (INCOMPLETE CORONARY INSUFFICIENCY) (ARTERIOSCLEROTIC HEART DISEASE)

AETIOLOGY:

- 1-Major cause (> 90%): Coronary atherosclerosis → incomplete gradual coronary occlusion. When the cause of chronic ischemia is atherosclerosis, the condition is called arteriosclerotic heart disease.
- 2-Less common causes of chronic ischemia
 - a) Paroxysmal tachycardia
 - b) Aortic incompetence or stenosis and all causes of low left ventricular output.
 - c) Syphilitic narrowing of coronary ostia.
 - d) Severe anemia

PATHOLOGY:

- 1-Patchy myocardial degeneration, necrosis leading to patchy fibrosis.
- 2-There may be also subendocardial fibrosis.
- 3-Valve fibrosis (in prolonged cases)

EFFECTS AND COMPLICATIONS:

- 1-Arrhythmias: due to affection of conductive system.
- 2-Angina pectoris: It is a clinical term denoting chest pain.

Definition: Attacks of retrosternal pain radiating to left shoulder. They develop after physical effort or psychological stress and disappear on rest.

Causes of angina pectoris:

 - a) All causes of chronic ischemia (see above)
 - b) Some causes of acute ischemia as shock & coronary artery spasm
- 3-Chronic heart failure: due to progressive fibrosis of the affected ventricle.
- 4-Coronary atherosclerosis predisposes to sudden complete occlusion.

B) ACUTE ISCHEMIA (COMPLETE CORONARY OCCLUSION)

AETIOLOGY:

- 1-Coronary atherosclerosis (over 90% of cases) complicated by complete coronary occlusion due to:
 - a) Advanced atherosclerotic lesions may be associated with remarkable coronary occlusion
 - b) Thrombosis developing over an atheroma.
 - c) Intimal hemorrhage under the atheroma → lifting of the atheroma → complete vascular occlusion. It is worth noting that the normally avascular intima becomes vascularized in atherosclerosis due to intimal angiogenesis. Hypertension (which often exists in cases of atherosclerosis) may cause rupture of intimal capillaries → hemorrhage → lifting of atheroma.
- 2-Rare causes include:
 - a) Severe coronary spasm
 - b) Severe hypotension (shock)
 - c) Coronary embolism
 - d) Polyarteritis nodosa complicated by thrombosis.
 - e) Dissecting aneurysm when it involves coronary ostia.
 - f) Thrombosis on top of syphilitic narrowing of coronary ostia.

EFFECTS AND COMPLICATIONS:

- 1-Sudden death (50%) due to ventricular fibrillation (a severe type of arrhythmia).
- 2-Myocardial infarction.
- 3-Acute heart failure

* L.V. more common
* R.V. rare due to right coronary occlusion

MYOCARDIAL INFARCTION

AETIOLOGY: Complete coronary occlusion (describe in details as above).

SITES:

- 1-Left Ventricle (LV) is much more commonly affected. Infarction may be:
 - Anterior infarct (anterior wall of LV, apex & anterior part of interventricular septum). It is due to occlusion of anterior descending branch of left coronary.
 - Lateral infarct (lateral wall of LV). It is due to occlusion of circumflex branch of left coronary.
 - Posterior infarct (posterior wall of LV). It is due to occlusion of a branch of the right coronary that supplies the posterior wall of LV.
- 2-Right Ventricle: Infarction is rare and is due to right coronary occlusion.

PATHOLOGY:

1-RECENT INFARCTION:

Gross Features: Gross changes appear after 6-8 hours from the onset of infarction

- 1-The infarct is swollen, pale, friable & may rupture. The margins are hyperemic.
- 2-Mural thrombus occurs.
- 3-Pericarditis develop. Fibrin covers the infarct surface.

Microscopic Features: Microscopic changes occur earlier than gross changes:

- 1-Coagulative necrosis of cardiac muscle → swollen eosinophilic muscle fibers, losing nuclei & striations.
- 2-Neutrophils appear followed by macrophages.

General Manifestations:

- 1-Leucocytosis.
- 2-Fever.
- 3-Rise of serum enzymes as lactate dehydrogenase, creatine phosphokinase (CPK) and serum glutamic oxaloacetate transaminase (SGOT).

Fate & complications:

- 1-Acute heart failure & ventricular fibrillation (VF). Death from cardiogenic shock is common.
- 2-Rupture of infarct → Hemopericardium & death.
- 3-Acute arrhythmias: may be severe (as VF) & fatal.
- 4-Systemic embolism from fragmented mural thrombus (aseptic embolism). May cause death.

2-HEALED INFARCTION

Gross Features: Fibrous healing occurs within few weeks (4-8 weeks according to infarct size)

- 1-The infarct appears thin grayish and fibrotic. It may dilate → cardiac aneurysm.
- 2-Mural thrombus is organized (fibrotic)
- 3-Pericardial fibrosis & adhesions

Microscopic Features: Necrotic muscles are engulfed by macrophages, followed by formation of granulation tissue and fibrosis

General Manifestations:

Disappear.

Fate & complications:

- 1-Chronic left ventricular failure → lung chronic venous congestion & pulmonary hypertension → right sided heart failure.
- 2-Rupture of cardiac aneurysm → Hemopericardium & death
- 3-Chronic arrhythmia e.g. extra systoles.

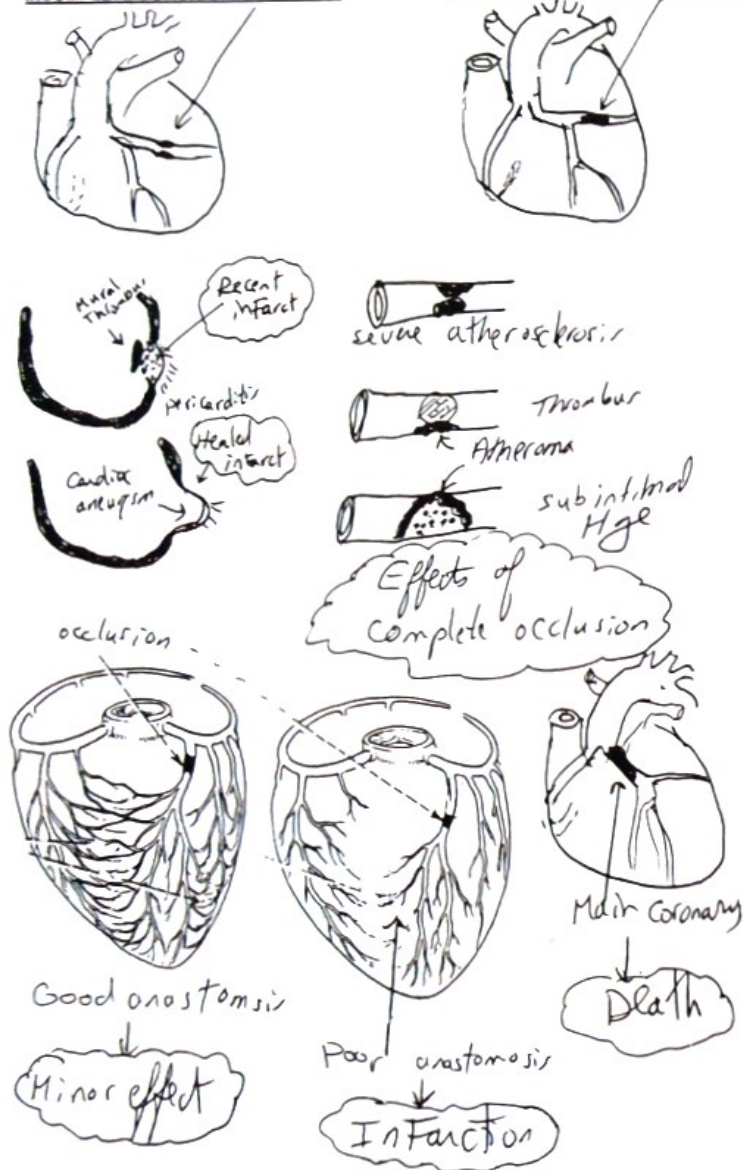
TYPES OF INFARCTION: ★

- 1-Transmural infarction: It involves the full thickness of the ventricular wall.
- 2-Subendocardial infarction: It is limited to the inner one third to one half of the myocardium. It may be due to vasospasm or hypotension without thrombosis. It is worth noting that the subendocardial part of the myocardium normally has less perfusion than the rest of the myocardium.

Freely you have received; freely give.

INCOMPLETE CORONARY OCCLUSION

COMPLETE CORONARY OCCLUSION



CONGENITAL HEART DISEASES B (x)

AETIOLOGY: One of the following during pregnancy:

- 1-Viral diseases as German measles.
- 2-Drugs as thalidomide.
- 3-Exposure to radiations.
- 4-Nutritional deficiencies
- 5-Syphilis

CLASSIFICATION: (TYPES):

A) NON-CYANOTIC GROUP:

- 1-Atrial Septal Defect (ASD).
- 2-Ventricular Septal Defect (VSD).
- 3-Patent Ductus Arteriosus.
- 4-Coarctation of Aorta.
- 5-Congenital Valve Stenosis: a)Aortic b)Pulmonary.

B) CYANOTIC GROUP:

- 1-Fallot's trilogi.
- 2-Fallot's tetralogy.
- 3-Eisenmenger's syndrome.
- 4-Transposition of great vessels.

ATRIAL SEPTAL DEFECT

- A pathological defect within the atrial septum → free communication between left and right-sided blood. It is a pathological condition, in contrast to patent foramen ovale which is an insignificant small slit like defect present in many normal individuals without functional disturbances.
- There is left to right shunt through the ASD.
- **Small ASD** → insignificant effects.
- **Large ASD** (3 cm) → hypertrophy & dilatation of the right side & sometimes cardiac failure.
- In advanced cases pulmonary hypertension occurs → reversal of the shunt (from right to left) → cyanosis (Eisenmenger's syndrome).
- Subacute infective endocarditis may develop at the edges of the defect

VENTRICULAR SEPTAL DEFECT

- 1-**Large defects (90% of cases):** They occur in the membranous part of the septum, just below the aortic valve. They lead to:
 - Left to right shunt → right-sided hypertrophy and dilatation (and sometimes failure).
 - Increased pulmonary flow leading to volume overload of the left side.
 - Eisenmenger's syndrome develops in advanced cases.
 - Subacute infective endocarditis may develop at the edges of the defect or in the mural endocardium of the right ventricle opposite the defect.
- 2-**Small defect (Roger's disease)** have minimal effects.

PATENT DUCTUS ARTERIOSUS

- Left to right shunt (from aorta to pulmonary artery) through the PDA → right-sided hypertrophy and dilatation, and sometimes failure.
- The increased pulmonary flow leads to left side volume overload → left side hypertrophy & dilatation.
- Eisenmenger's syndrome (reversal of the shunt) may develop in advanced cases.
- Subacute infective endocarditis may occur.

COARCTATION OF AORTA

This is congenital narrowing of an aortic segment. Two types:

- 1-**Infantile Type** (Preductal Type): The narrow aortic segment is proximal to a patent ductus arteriosus. Blood passes from the pulmonary artery to the aorta through the PDA. The infant dies shortly after birth.
- 2-**Adult Type:** The narrow segment is distal to a closed ductus arteriosus. Effects include:

- **Hypertension** in the upper part of the body (arms, head and neck). Death may occur due to:
 - Left sided heart failure.
 - Cerebral hemorrhage.
 - Rupture of aorta.
- **Hypotension** in the lower part of body (legs).
- Opening of **arterial collaterals** between aortic branches proximal & distal to obstruction

CONGENITAL STENOSIS OF VALVES

1-**Congenital pulmonary stenosis**:

- Isolated form: It leads to concentric hypertrophy of the right ventricle.
- As a part of Fallot's triology or tetralogy (see later).

2-**Congenital aortic stenosis** leads to concentric hypertrophy of the left ventricle.

FALLOT'S TRILOGY

It consists of:

- 1) ASD
- 2) Pulmonary stenosis.
- 3) Right ventricular hypertrophy.

Manifestations:

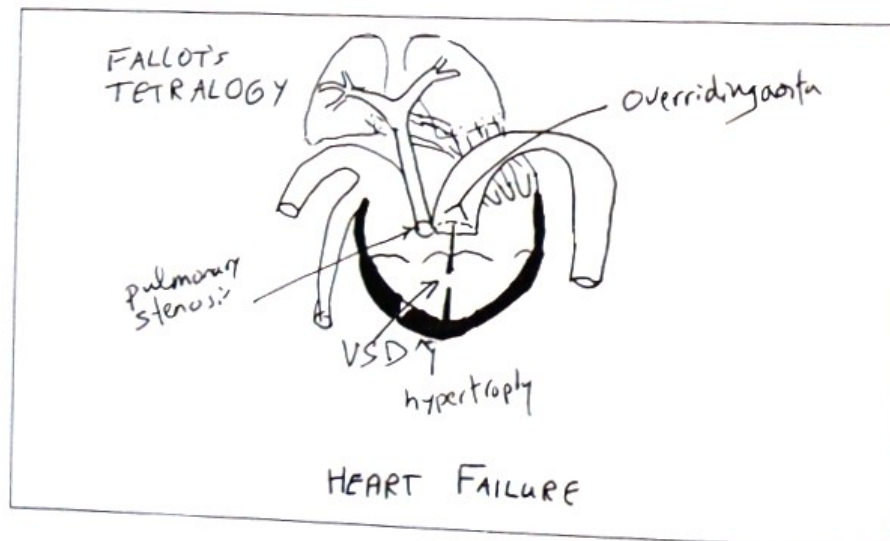
High right sided pressure due to pulmonary stenosis → right to left shunt through ASD → cyanosis → secondary polycythemia and clubbing of fingers.

★ FALLOT'S TETRALOGY ★

It consists of:

- 1) VSD. *ventricular septal defect*
- 2) Pulmonary stenosis.
- 3) Right ventricular hypertrophy.
- 4) Over-riding aorta receiving blood from both ventricles (leading to cyanosis).

Manifestations: Cyanosis, secondary polycythemia and clubbing of fingers.



HEART FAILURE

DEFINITION: This is failure of the ventricular contractions to maintain sufficient cardiac output to meet the body demands.

TYPES OF HEART FAILURE: Two types ; acute and chronic:

ACUTE HEART FAILURE

AETIOLOGY:

- 1-Acute myocardial damage: a)Recent myocardial infarction. b)Myocarditis.
- 2-Massive pulmonary embolism (acute right sided failure).
- 3-Haemopericardium → heart compression → decreased diastolic filling → decreased cardiac output.

EFFECTS: Acute congestion and oedema (pulmonary and / or generalized).

CHRONIC HEART FAILURE

PATHOGENESIS:

1-STAGE OF COMPENSATION: The heart maintains adequate cardiac output by:

- Slight dilatation of the affected chamber → slight stretch of myocardial fibers → stronger contractions.
- Compensatory hypertrophy occurs → stronger contractions.
- Increased heart rate → increased tissue perfusion.

2-STAGE OF DECOMPENSATION (FAILURE):

Decompensation (heart failure) is due to marked dilatation of the affected ventricle & cardiac fatigue. The mechanism includes:

- Prolonged increase in heart rate → cardiac fatigue..
- Myocardial hypertrophy is not accompanied by increase of myocardial capillaries → relative ischemia → gradual fibrosis → weakening and dilatation.
- Dilatation leads to overstretch of myocardial fibers → weaker contractility.

TYPES OF CHRONIC HEART FAILURE:

1-LEFT SIDE HEART FAILURE:

Aetiology:

- 1-Hypertension.
- 2-Coronary heart disease:
 - Healed infarct.
 - Arteriosclerotic heart disease.
- 3-Valve disease: Aortic stenosis, aortic incompetence, mitral incompetence.
- 4-Congenital diseases as coarctation of aorta.

Pathological features:

- 1-Hypertrophy and dilatation of left atrium and left ventricle.
- 2-Attacks of acute pulmonary oedema and dyspnea on lying down (cardiac asthma) and on exertion.
- 3-Chronic lung congestion leading to pulmonary hypertension and then right sided heart failure.
- 4-Manifestations of low cardiac output as oliguria.

2-RIGHT SIDE HEART FAILURE:

Aetiology:

- 1-Causes in the left side of heart :
 - Mitral stenosis.
 - Left sided heart failure.
- 2-Causes in the right side of the heart:
 - Pulmonary stenosis
 - Tricuspid incompetence.

3-Congenital heart diseases as ASD and VSD.

4-Cor pulmonale (right side H.F. caused by lung diseases) due to:

- Lung fibrosis due to pulmonary tuberculosis, pulmonary bilharziasis.
- Emphysema.

Pathological features:

1-Hypertrophy and dilatation of right atrium and right ventricle.

2-Chronic general venous congestion (generalized oedema, hypoxia, cyanosis, nutmeg liver...etc.).

3-Low cardiac output.

Remark: Combined left and right side heart failure is called congestive heart failure because there is congestion of the whole body including the lungs.

TUMORS OF HEART

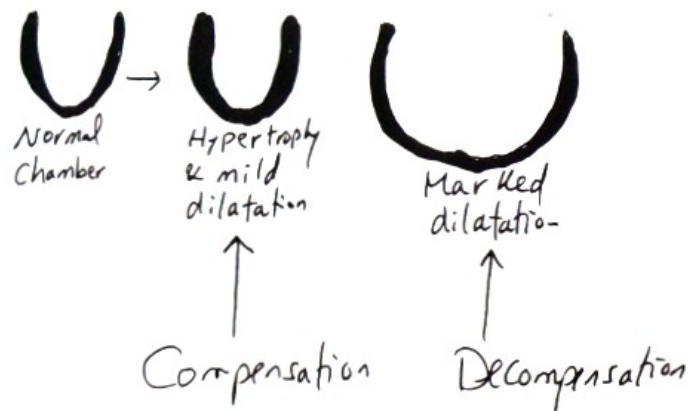
BENIGN TUMORS OF HEART: Myxoma, Rhabdomyoma, Fibroma, Lipoma (see general pathology)

MALIGNANT TUMORS OF HEART: (see general pathology)

1-Primary: Rhabdomyosarcoma, Angiosarcoma.

2-Metastatic tumors (rare) e.g. from bronchogenic carcinoma, lymphoma, leukemia or malignant melanoma

HEART FAILURE



DISEASES OF BLOOD VESSELS

ARTERIOSCLEROSIS

2011 TLO

This is thickening and hardening of arterial walls. Arteriosclerosis includes

- Atherosclerosis
- Monckeberg's sclerosis (medial calcification)
- Arteriolosclerosis

ATHEROSCLEROSIS (ATHEROMA)

DEFINITION:

Atherosclerosis: This is patchy thickening of the intima of arteries by lesions composed of deposited lipids surrounded by proliferated connective tissue. Each of these lesions is called atheroma.

PREDISPOSING RISK FACTORS:

1-High level of plasma lipids (hyperlipidemia):

This is a major risk factor. The total plasma cholesterol or low density lipoprotein (LDL) correlate strongly with the severity of atherosclerosis. Triglycerides play a less significant role than LDL (cholesterol). Hyperlipidemia may be:

- Hereditary.
- Dietary (obesity) or
- Metabolic (diabetes).

2-Local vascular stress: This is important as evidenced by:

- Hypertension** is a major risk factor. The importance of blood pressure in the pathogenesis of atherosclerosis explains why under normal conditions atherosclerosis does not occur in veins or pulmonary arteries (due to low pressure). It has also been found that pulmonary atherosclerosis develops in cases of pulmonary hypertension.
- Eddy currents:** Atherosclerotic lesions are more extensive around ostia of aortic branches; reflecting the significance of the local stress factors created by eddy turbulent currents that normally occur in these sites.

3-**Smoking** is a major risk factor. Cessation of smoking dramatically reduces the risk.

4-**Diabetes mellitus:** It leads to hypercholesterolemia.

5-**Heredity (familial predisposition):** More than one genetic factor.

6-**Sex:** Females are less commonly affected. They are protected by their estrogen, therefore atherosclerosis can develop after the menopause.

7-**Age:** The lesions may start to develop during childhood, but they are not severe enough to cause clinical disease except after middle age.

8-**Diet:** See above for hyperlipaemia

9-**Syphilitic aortitis** (rare).

PATHOGENESIS:

Chronic endothelial injury (caused by vascular stress as in hypertension or by the toxic products of cigarette smoking) → allows trapping of LDL in the subendothelial part of the intima to which platelets, lymphocytes & monocytes adhere and release cytokines (as TNF & IL-1) & growth factors (as PDGF) leading to:

- Oxidation of soluble LDL → insoluble oxidized LDL → further endothelial injury & further adherence of platelets & monocytes, together with more cytokine & growth factors production.
- Migration & proliferation of smooth muscle cells from media to intima.
- Proliferation of fibroblasts & deposition of collagen and extracellular matrix.
- The process is progressive

PATHOLOGICAL FEATURES:

Distribution (Sites):

- 1-Large arteries: Aorta and its main branches
- 2-Small arteries (coronaries, cerebral and renal arteries).
- 3-The medium-sized arteries as femoral artery are less severely affected.

Gross Features:

1-Intimal Lesions:

- **Fatty Streaks** usually start in children and represent an important precursor of the subsequent atheromatous plaques. They appear as soft slightly raised yellow elevations. They are due to deposition of LDL in the subendothelial layer of the intima.
- **Atheromatous Plaque (Atheroma):** These are the main lesions and appear as firm raised yellowish white plaques & nodules. They are due to fibrosis developing around deposited lipids. They may become hard due to dystrophic calcification.
- **Atheromatous Ulcers:** Necrosis of the endothelium covering the atheromatous plaques → irregular ulcers are irregular with sharp edges. They may show dystrophic calcification & get covered by thrombi

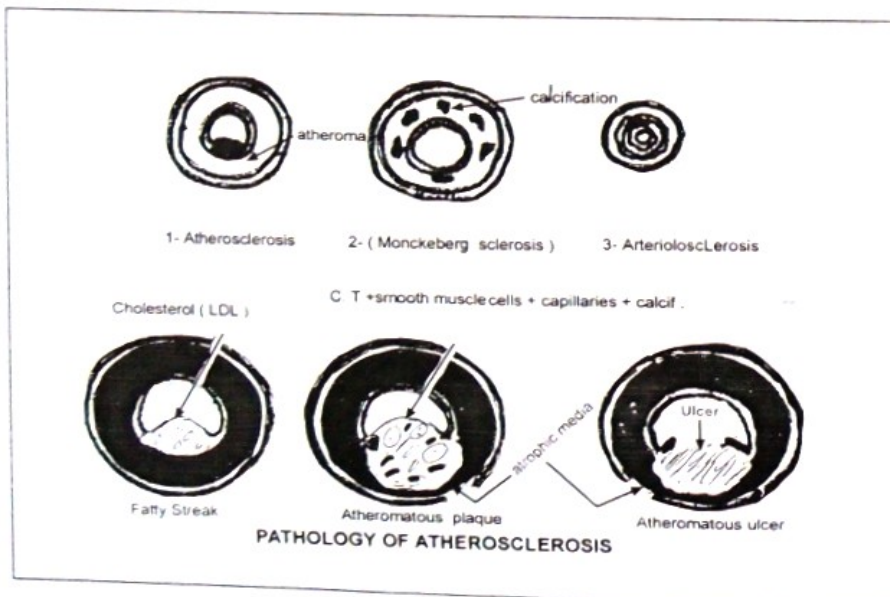
2-The Media: Media under the intimal lesions appears thin and atrophic (pressure atrophy).

Microscopic Features:

1-Intimal Lesions:

- **Fatty Streaks:** The subendothelial part of intima shows lipids. The dissolved cholesterol crystals appear in paraffin sections in the form of needle shaped clear clefts. There are also foam cells (macrophages engulfing lipid).
- **Atheromatous Plaque (Atheroma):** The subendothelial part of the intima shows:
 - Lipids (dissolved needle shaped cholesterol clefts) & macrophages (foam cells)
 - Vascularization: Capillaries are derived from the endothelial part of intima or from vasa vasorum
 - Proliferated connective tissue (fibrosis) & smooth muscle cells
 - Dystrophic calcification may occur and appears as dark blue granules.
- **Atheromatous Ulcers:** As atheromatous plaque + necrosis of overlying endothelium.

2-The Media: Atrophy (thinning) and fragmentation of internal elastic lamina occurs opposite the intimal lesions.



EFFECTS AND COMPLICATIONS:

1-ISCHAEMIA: Incomplete or complete:

- **In small arteries:** Ischaemia may be incomplete due to atherosclerotic narrowing of the arteries or complete due to superimposed thrombus or subintimal haemorrhage elevating the atheroma. Examples:
 - a- Coronaries:
 - Narrowing → arteriosclerotic heart disease.
 - Occlusion → myocardial infarction.
 - b- Femoral artery:
 - Narrowing → intermittent claudications.
 - Occlusion → dry gangrene
- **In large arteries (aorta)** thrombosis may develop over atheromata and this may be complicated by systemic embolism leading to infarcts in different organs.

2-ANEURYSMS: They are due to stretch of atrophic media:

- **In small arteries:** The commonest is the cerebral arteries.
- **In aorta:** They may be fusiform or dissecting (see later).

MONCKEBERG'S SCLEROSIS (MEDIAL CALCIFICATION)

Definition: This is calcification of media of medium sized arteries of elderly persons

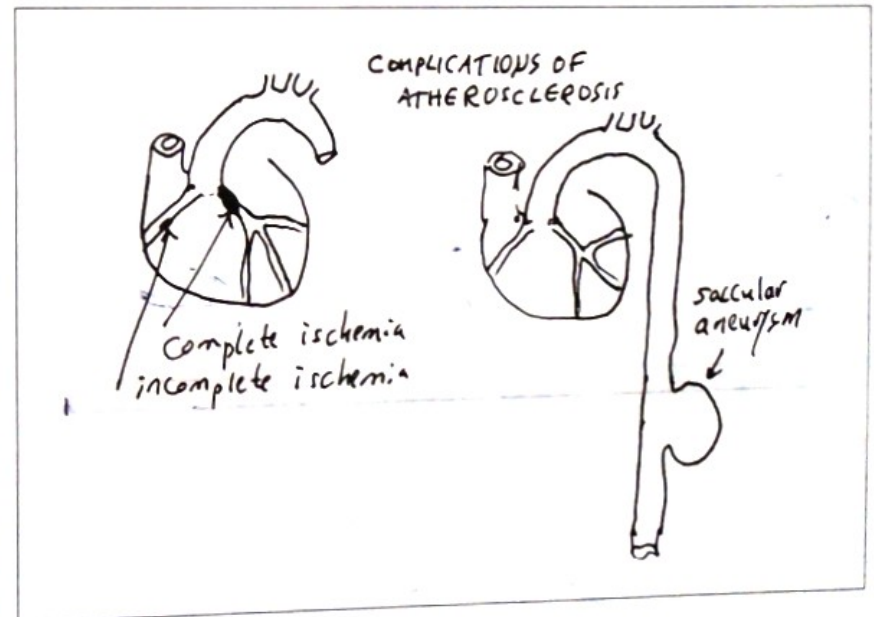
Gross: Hard rigid arterial wall without lumen narrowing. Atherosclerosis may coexist since the lesions occurs in old age where atherosclerosis is common.

Microscopy: Hyaline degeneration of media with patchy deposition of calcium.

Clinical significance: These lesions are insignificant (don't encroach on the vessel lumen)

ARTERIOLOSCLEROSIS

This is thickening and narrowing of arterioles and small arteries occurring in cases of hypertension and diabetes mellitus (see pathology of hypertension)



HYPERTENSION (A)

DEFINITION:

Persistent elevation of blood pressure above normal.

TYPES OF HYPERTENSION:

1- SECONDARY HYPERTENSION: (10%)

Aetiology: Secondary hypertension may be caused by:

- a) **Renal Diseases** as glomerulonephritis, pyelonephritis, hydronephrosis, polycystic disease...etc
- b) **Endocrine Diseases** as pheochromocytoma, 1ry aldosteronism, Cushing syndrome.
- c) **Vascular and blood diseases** as coarctation of aorta and polycythaemia vera.

Pathological Features: May be classified into benign and malignant hypertension.

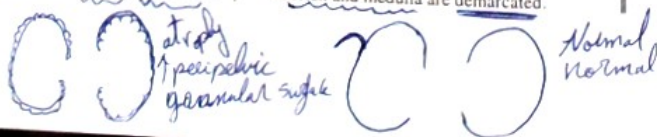
2- PRIMARY (ESSENTIAL) HYPERTENSION: (90%)

Aetiology:

- a) **Genetic Factor:** Essential hypertension is a familial (inherited) disease.
- b) **Neurogenic mechanism:** The susceptible individuals are characterized by a high sympathetic tone & chronic stress leading to considerable vasoconstriction of peripheral arterioles.
- c) **Humoral mechanism:** Renal ischemia (due to vasoconstriction of renal arterioles) leading to renin secretion which activates plasma angiotensinogen producing angiotensin, thus vasoconstriction of peripheral arterioles occurs.
- d) **Other helping factors:** i) Excess salt in diet ii) obesity.

Pathological Features of essential hypertension: Benign & malignant types:

BENIGN ESSENTIAL HYPERTENSION	MALIGNANT ESSENTIAL HYPERTENSION
-Commonest type of hypertension. -Usually above the age of 40. -Slowly progressive rise of blood pressure -Long course (30 years or more).	-Rare. -Usually in younger ages (25-35 years). -Rapidly progressive rise of blood pressure -Short fatal course.
PATHOLOGY	
1-VASCULAR LESIONS (ARTERIOLOSCLEROSIS)	
BENIGN ARTERIOLOSCLEROSIS: Walls of small arteries and arterioles & (sometimes larger arteries) show: ① Hyalinosis of intima and media leading to thickening & narrowing of these vessels. ② Elastosis: The internal elastic lamina splits into many layers. REMARK: In addition to arteriosclerosis, atherosclerosis is also common.	MALIGNANT ARTERIOLOSCLEROSIS: Walls of small arteries and arterioles show: ① Arteriolar fibrinoid necrosis: Collagen of the arteriolar wall is fragmented, accompanied by inflammation and sometimes thrombosis. ② Concentric hyperplasia of connective tissue & smooth muscle cells → thickening & narrowing. ③ Hyalinosis and elastosis are milder than in benign arteriosclerosis (due to short disease course).
2-BILATERAL KIDNEY LESIONS (NEPHROSCLEROSIS)	
BENIGN NEPHROSCLEROSIS: GROSS: Both kidneys show: • Size: Small (1ry contracted kidney). • Surface: Finely granular. • Capsule: Adherent and strips with difficulty leading to decortication. • Cutsection shows: -Cortex and medulla are fibrotic, atrophic &	MALIGNANT NEPHROSCLEROSIS: GROSS: Both kidneys show: • Size: Normal. • Surface: Smooth. • Capsule: Strips easily. • Cutsection shows: -Cortex and medulla are demarcated.



-not demarcated from each other. -Thick prominent arterioles. -Increased peripapillary fat. -Small cysts	-They show haemorrhagic foci. -Thick prominent arterioles. -Normal peripapillary fat
MICROSCOPY:	MICROSCOPY:
• Afferent and efferent arterioles show benign arteriosclerosis (describe). • Glomeruli show gradual ischaemic atrophy, fibrosis and hyalinosis. • Tubules: a) Atrophy of nonfunctioning tubules related to atrophic glomeruli. b) Compensatory cystic dilatation of tubules related to functioning glomeruli.	• Afferent arterioles show malignant arteriosclerosis (describe). • Glomeruli show necrosis and hemorrhage. • Tubular atrophy is focally detected.
3- HEART LESIONS:	
Marked concentric hypertrophy of left ventricle. The interventricular septum bulges towards the right ventricle. Heart failure (describe) & is the cause of death in 60% of cases.	Mild left ventricular hypertrophy (due to short course of the disease).
4- RETINAL LESIONS (hypertensive retinopathy):	
Thickening (arteriosclerosis) of retinal arterioles → compression of venules. Effects: papilledema, retinal haemorrhages & exudates (seen as cotton-wool spots in funduscopic examination).	
5- BRAIN LESIONS:	
Microaneurysms of small cerebral arteries. Cerebral thrombosis & haemorrhage may occur (strokes).	
CAUSES OF DEATH:	
Heart failure (60%), cerebral Hge (30%), chronic renal failure (10%).	Acute renal failure (95%), cerebral Hge or heart failure.

ARTERITIS

(Arterial Wall Inflammation)

BUERGER'S DISEASE (THROMBOANGIITIS OBLITERANS)

Definition:

This is segmental inflammation of medium & small arteries that spreads to adjacent veins & nerves. The disease affects heavy smoking, middle-aged males. Extremities are the main sites.

Pathology: The arterial walls show acute & chronic inflammation associated with thrombosis. Thrombi undergo organization and recanalization.

Effects & complications:

- a- Intermittent claudications
- b- Gangrene.

COLLAGEN DISEASES OF ARTERIES

1-POLYARTERITIS NODOSA

Definition: It is an autoimmune collagen disease affecting medium-sized and small arteries of any organ except the lung (heart, brain, kidney, GIT...etc). Males are more commonly affected.

Pathology: The wall of the affected artery shows multiple small nodular swelling (reddish gray nodules; each about 2-4 mm). Microscopically these nodules consist of fibrinoid necrosis, eosinophils, neutrophils, and mononuclear leucocytes. Fibrosis develops gradually.

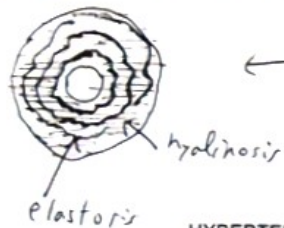
Effects & complications:

- a) Thrombosis and infarcts.
- b) Mycotic aneurysms due to dilatation of the weak fibrotic parts.
- c) Hemorrhage due to rupture of the aneurysms.

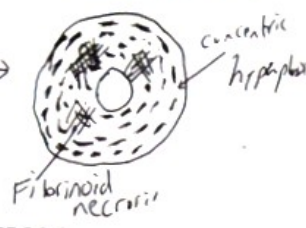
polyarteritis nodosa
autoimmune disease
common for Autoimmune disease

HYPERTENSIVE ARTERIOLOSCLEROSIS

BENIGN ARTERIOLOSCLEROSIS



MALIGNANT ARTERIOLOSCLEROSIS



HYPERTENSIVE NEPHROSCLEROSIS

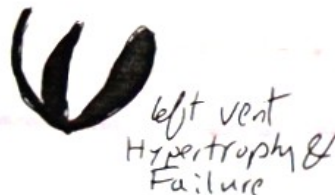
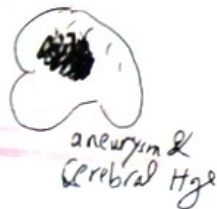
BENIGN NEPHROSCLEROSIS



MALIGNANT NEPHROSCLERIS



OTHER EFFECTS OF HYPERTENSION



2-SYSTEMIC LUPUS ERYTHEMATOSUS (SLE):

Definition: A fairly common multisystem autoimmune collagen disease

Sex: Female are much more commonly affected. Female to male ratio is 10:1

Pathogenesis: The main autoantibodies are antinuclear antibodies (ANAs). Genetic predisposition and exogenous factors such as drugs, ultraviolet radiation & virus infections may all contribute to the mechanism of autoimmunity.

Pathological Features:

a-Acute Necrotizing Vasculitis: This occurs in all tissues. It affects small arteries & arterioles which show fibrinoid necrosis, accompanied by perivascular lymphocytic infiltrates. At this early acute phase, anti DNA antibodies together with complement (C3) are found within the fibrinoid deposits. Later, these vessels undergo fibrous thickening & narrowing.

b-Kidney Lesions: Glomerular involvement is variable. The severest forms lead to nephrotic syndrome and renal failure. For details see chapter VI

c-Skin rash: A maculopapular rash, usually in the butterfly area of the face (bridge of nose and malar eminences).

d-Serous membranes: Serofibrinous inflammation of the dry and wet types.

e-Heart lesions:
- Nonbacterial atypical verrucous endocarditis (Libman-Sacks endocarditis) affecting any Valve which shows small warty lesions (1-3 mm each) composed of fibrinoid deposits, inflammatory cells & later fibrosis.

- Myocarditis

- Pericarditis

f-Joints: inflammation, however, strikingly no joints deformities occur.

g-Other organs and tissues may be affected. The essential lesion is acute vasculitis.

h-Hematoxylin bodies Basophilic nuclear fragments (due to ANAs) seen in many SLE lesions.

OTHER TYPES OF ARTERITIS

1-Wegener's Granulomatosis: A serious disease of unknown pathogenesis, characterized by:

a-Necrotizing granulomas of the upper and/or lower respiratory tract

b-Necrotizing vasculitis of small arteries and veins.

c-Necrotizing (often crescentic) glomerulonephritis

2-Temporal Arteritis (Giant cell arteritis): Unknown pathogenesis; possibly autoimmune, characterized by segmental granulomatous inflammation of arteries of the head, particularly branches of the carotid artery

ANEURYSMS

TRUE ANEURYSMS

DEFINITION: Localized dilatation of the arterial wall.

AETIOLOGY:

1) Weakening Of Media:

a)Congenital: At the bifurcation of the arterial wall

b)Atherosclerosis: Abdominal aorta and cerebral arteries are the commonest.

c)Inflammatory as in cases of:

• Subacute infective endocarditis

• Polyarteritis nodosa

• Syphilitic aneurysm of thoracic aorta

• Aneurysm of pulmonary artery in cases of bilharziasis.

d)Medionecrosis.

2) Hypertension is a helping factor.

weak media @ Hypertension

* Female Common 10:1

600 autoantibody

80% ANA

Libman-Sacks

discuss Burger's

Wegener's

Burger's
Common in
affect nerve
* Necrotizing
arteritis

* Crescentic
necrosis

White Knight

EXAMPLES, TYPES AND PATHOLOGY:

1) **Congenital (Berry) Aneurysms:** These are multiple small aneurysms at the bifurcation of cerebral arteries in the circle of Willis. They are due to congenital absence of the media. Their rupture leads to cerebral or subarachnoid hemorrhage.

2) **Atherosclerotic Aneurysms:** The aneurysm is large and fusiform. The most common sites are the abdominal aorta & cerebral arteries. It may lead to pressure effects (e.g. pressure atrophy of adjacent vertebrae). It may also be complicated by thrombosis or rupture.

3) **Syphilitic Aneurysm:** A large saccular or fusiform aneurysm of thoracic aorta (see general pathology).

4) **Bilharzial Pulmonary Aneurysm:** See general pathology.

5) Mycotic Aneurysms:

These are small inflammatory aneurysms affecting the small arteries; mainly the cerebral, mesenteric and coronary arteries. They are seen in cases of

- Subacute infective endocarditis
- Polyarteritis nodosa.

They are due to inflammatory weakening and fibrosis of the media which stretches under arterial pressure leading to aneurysms.

Thrombosis and ischemia are common complications.

6) **Dissecting Aneurysm:** Uncommon. Affects aorta at old ages. May be due to:

a) Medionecrosis:

This occurs in old age. Focal necrosis of the musculoelastic tissue of the media leads to rupture of the vasa vasorum. The resulting intramural hemorrhage leads to splitting (dissection) of the media in two layers.

Dissection may progress to the level of coronary or other aortic branches leading to obstruction of the lumen of these branches, by the inner layer of the dissecting aneurysm and this leads to serious ischemic effects.

If before this happens, the inner layer ruptures, the condition becomes ameliorated. If the whole aneurysm ruptures, the condition is fatal.

b) **Atherosclerosis:** Blood may pass through a crack in an atheromatous ulcer → medial splitting (dissecting aneurysm) → may progress to involve aortic branches (see before)

COMPLICATIONS OF TRUE ANEURYSMS:

- Pressure on surroundings.
- Thrombosis and embolism.
- Rupture and hemorrhage.

FALSE ANEURYSMS

The wall of the aneurysm is not a part of the arterial wall but consists of fibrous tissue. False aneurysms are caused by trauma. Types include:

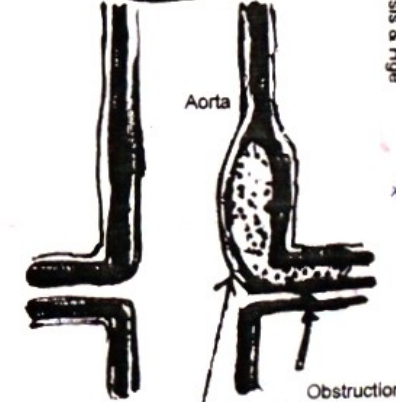
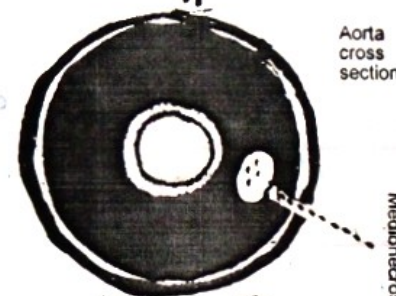
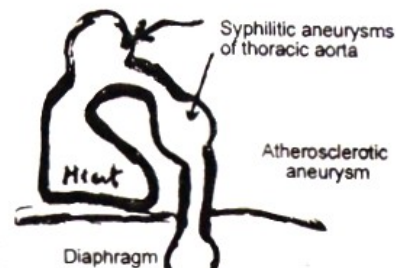
1) **SIMPLE FALSE ANEURYSM (PULSATING HAEMATOMA):** due to trauma + fibrous Periaarterial hematoma due to traumatic arterial injury may be followed by fibrous organization occurring at its periphery and this leads to false aneurysm.

2) **ARTERIOVENOUS ANEURYSMS (ARTERIOVENOUS FISTULAE):** artery and vein Causd by injury of an artery and its adjacent vein. Two types of arteriovenous fistula:

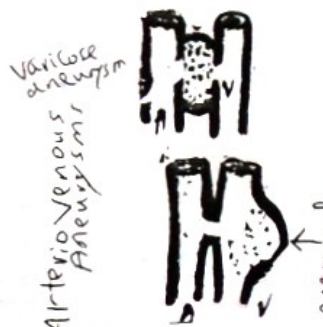
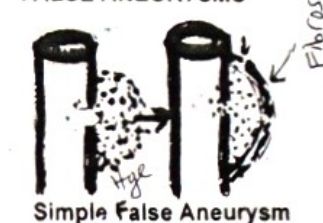
a) **Varicose aneurysm:** Hematoma between artery and vein undergoes peripheral organization leading to false aneurysm attached to both artery and vein.

b) **Aneurysmal Varix:** Direct communication of artery and vein without an intervening sac. The vein shows aneurysm-like dilatation opposite this communication.

ANEURYSMS



FALSE ANEURYSMS



old age → focal necrosis in musculoelastic tissue of media
→ rupture of vasa vasorum which are arteries & veins supplying blood vessel

→ Intramural haemorrhage
→ split media 2 layers

* If Dissection progress to level of coronary or aortic branches
→ obstruction of lumen by inner layer of dissecting aneurysm
→ serious ischemic effects

* Before this happen inner layer rupture become ameliorated if whole aneurysm rupture = fatal

VARICOSE VEINS

DEFINITION:

Dilatation, elongation, thickening and tortuosity of veins.

AETIOLOGY AND SITES:

1-Non-obstructive type:

Common in long-shaft saphenous vein
Affected veins: Mainly long saphenous vein due to prolonged standing (as in policemen), pampiniform plexus (varicocele) or in hemorrhoidal veins (piles).

Predisposing factors

- a) Congenital weakness of the venous wall
- b) Incompetence of venous valve
- c) Acquired weakness of venous walls as in senility & obesity.

2-Obstructive type:

- a) Central obstruction (right sided heart failure): varicosities of leg veins, varicocele, piles.
- b) Portal obstruction (in cases of cirrhosis or hepatic bilharziasis): oesophageal varices, external piles and caput medusae.
- c) Peripheral obstruction e.g.:
 - Leg veins in case of pregnancy due to uterus compression
 - Piles in case of cancer rectum.
 - Left varicocele in case of renal carcinoma of left kidney.

COMPLICATIONS:

- 1-Phlebothrombosis → Congestion and oedema. = Aseptic thrombus in vein, not inflamed
- 2-Thrombophlebitis → Pyaemia. septic thrombus in inflamed vein, not inflamed
- 3-Varicose ulcers in the lower limbs due to pressure atrophy of the overlying skin
- 4-Rupture of the varicosity → hemorrhage.

TUMORS OF BLOOD VESSELS

BENIGN TUMORS OF VESSELS: (see general pathology)

- 1-Capillary hemangioma.: see general pathology.
- 2-Cavernous hemangioma.: see general pathology.
- 3-Glomangioma. A rare benign vascular tumor, less than 1 cm, extremely painful, most commonly occurs beneath the nails. It consists of branching vascular spaces surrounded by glomus cells (specialized cells with a neuromyoarterial receptor sensitive to temperature & regulates arteriolar flow).

MALIGNANT TUMORS OF VESSELS:

1-ANGIOSARCOMA:

This is the most malignant vascular neoplasm. Skin, breast, liver, spleen and soft tissue are the most common sites. Grossly the tumor ranges between small red nodules and large grayish fleshy masses. Microscopically, it consists of malignant endothelial cells. In the better-differentiated tumors, vascular lumens may be formed in relation to tumor cells.

2- KAPOSI'S SARCOMA (KS):

Gross picture: The tumor affects skin & viscera. It appears as multiple purple patches or nodules.

Microscopic picture: The characteristic lesion consists of well-formed endothelium-lined vascular channels, mixed with sheets of plump spindle cells with intervening slit-like vascular spaces filled with erythrocytes. The pathogenesis of the tumor is unclear.

Types of Kaposi's sarcoma:

- a) Classic/European KS: Occurs in elderly men. The lesions consist of multiple cutaneous and less commonly visceral nodules. It rarely causes death.

KS is rare

b) African KS: Similar to European KS but occurs in younger men.

c) Transplant-associated KS: It develops in transplanted patients receiving immunosuppressive therapy. There is wide cutaneous & visceral involvement. Lesions regress when immunosuppression is discontinued.

d) AIDS-associated KS: It develops in patients suffering from AIDS, particularly homosexuals. There is cutaneous and visceral involvement. The lesions respond to cytotoxic chemotherapy or alpha-interferon.

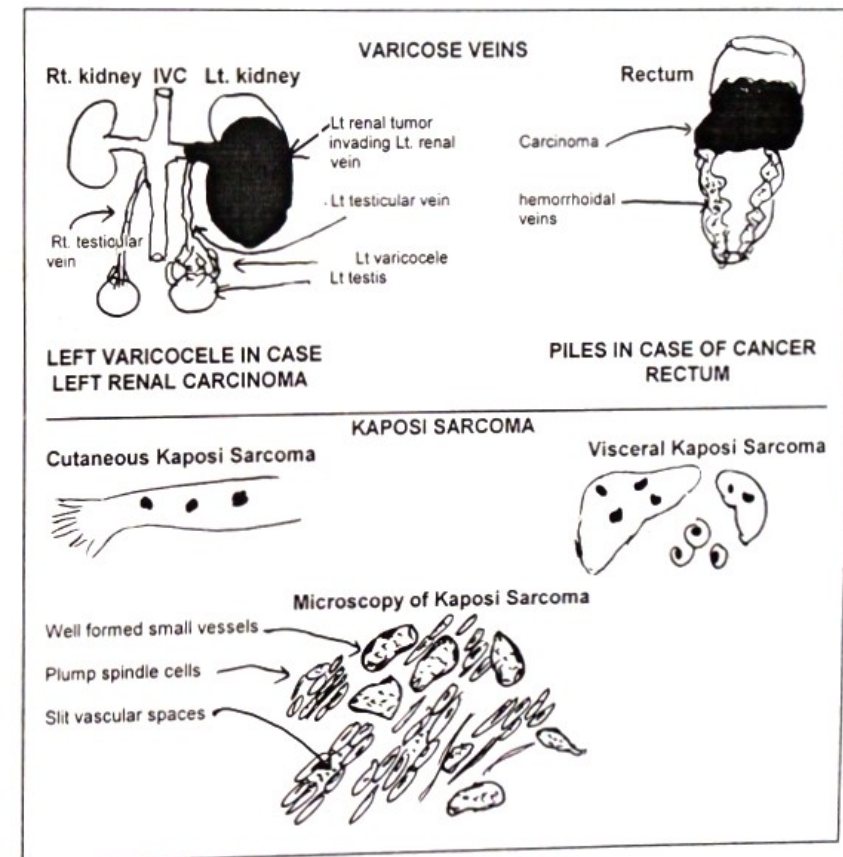
3- HEMANGIOENDOTHELIOMA:

A low grade (intermediate) malignant vascular tumor composed of vascular channels lined by endothelial cells (spindle type or epithelioid type) showing low grade atypia. The tumor grows slowly and its prognosis is much better than the other malignant vascular neoplasms. It may be cured by excision. Recurrences occur in 40% of cases and metastases develop late in about 20% of cases.

4- HEMANGIOPERICYTOMA:

A low grade (intermediate) malignant arises from cells around blood vessels (pericytes)

5- MALIGNANT GLOMUS TUMOR: Extremely rare



Systemic infection
33 chronic non-specific

التهاب الحنجري مزمن
لا نسيجي
أو التهاب الحنجري المزمن

* Pathology: Acute → Macro = suppurative
Vascular = V.D. + Acute inflammation
= V.D. + Acute inflammation + polypoid
Causal (for) mal-epithelium + polypoid
Swollen edematous + suppurative covered with mucous
pink membrane + granular mucous
covered with granular mucous
polypoid

DISEASES OF THE UPPER RESPIRATORY SYSTEM

THE UPPER RESPIRATORY TRACT (URT):
It consists of: 1) Nose, nasal sinuses & nasopharynx 2) Tonsils 3) Larynx 4) Middle ear
Diseases of the URT are clinically referred to as diseases of Ear, Nose & Throat (ENT)

DISEASES OF NOSE, SINUSES & PHARYNX

RHINITIS

Definition: Rhinitis is inflammation of the nasal mucosa. Usually accompanied by sinusitis
Types:
I) Acute Rhinitis: 1-Acute catarrhal rhinitis
2-Acute allergic rhinitis
II) Chronic Rhinitis: 1-Chronic nonspecific rhinitis
2-Chronic granulomatous (specific) rhinitis:
a) Bacterial as rhinoscleroma, tuberculosis, leprosy, syphilis
b) Fungal as rhinosporidiosis
c) Parasitic as leishmaniasis
d) Sarcoidosis

ACUTE CATARRHAL RHINITIS

Definition: Inflammation of the nasal cavity
Aetiology:
1-Rhinoviruses, which may be followed by secondary bacterial infection
2-Exposure to cold is an important predisposing factor.
Pathology: Catarrhal inflammation (see general pathology).
Complications: Spread of infection → sinusitis, pharyngitis, adenoids, laryngitis, otitis media, bronchitis, bronchopneumonia...

ACUTE ALLERGIC RHINITIS

An atopic disease (type I hypersensitivity) caused by inhalation of certain antigens (as pollens) → allergic inflammation rich in eosinophils. Repeated attacks (chronicity) of allergic rhinitis & sinusitis → nasal polyps.

NASAL POLYPS

Aetiology: Repeated attacks of allergic rhinitis and sinusitis.
Gross: Multiple soft pink polyps, projecting from the mucosa of the nose and sinuses.
Microscopy: The polyp consists of:
1-Pseudostratified ciliated epithelial covering. Squamous metaplasia is common.
2-Connective tissue core showing congested capillaries, oedema, many eosinophils, many plasma cells and proliferated mucous glands.
Complications:
1-Nasal obstruction: This predisposes to infection leading to chronic rhinitis and sinusitis.
2-Epistaxis.

CHRONIC NONSPECIFIC RHINITIS

The condition is predisposed to by nasal obstruction (e.g. nasal polyps, deviated nasal septum) → mucous retention which favors bacterial infection. Retention of exudates due to nasal obstruction favors chronicity.

* Complication of acute rhinitis
→ chronicity
→ spread

Pathology: The affected mucosa shows chronic inflammatory changes, endarteritis & fibrosis.
Types Of Chronic Nonspecific Rhinitis:
a) Simple (nonthickened mucosa).
b) Hypertrophic: Mucosa is thickened & polypoid.
c) Atrophic: see below.

ATROPHIC RHINITIS

Aetiology: This is a rare chronic condition affecting females more commonly than males. The pathogenesis is unclear. The suspected factors include ischemic changes due to endarteritis occurring in cases of chronic nonspecific rhinitis, endocrinal disturbances and infection with Klebsiella ozaenae.

Pathology: The nasal mucosa is thin and atrophic. The nasal cavity is widened. An offensive discharge is common. There is anosmia (loss of smell) due to atrophy of nerve endings.

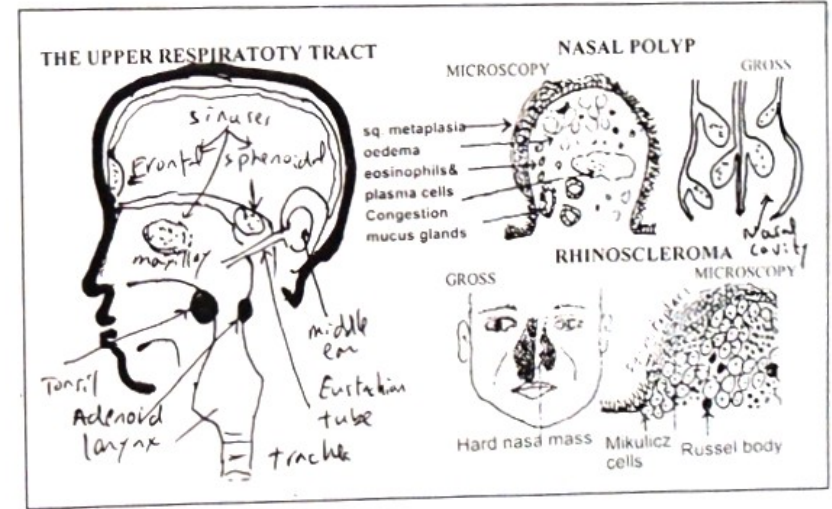
SCLEROMA (RHINOSCLEROMA)

Aetiology:
A common disease in Egypt caused by klebsiella rhinoscleromatis. Nose is the most common site (rhinoscleroma), but pharynx (pharyngoscleroma), larynx (laryngoscleroma) & upper trachea may be also affected.

Pathology:
Gross Features: Single or multiple hard nodular swelling filling the nasal cavity & may extend to upper lip, sinuses, pharynx, larynx & upper trachea.

Microscopy:
1-The covering nasal mucosa may show squamous metaplasia.
2-The submucosa is densely infiltrated with inflammatory cells & shows progressive fibrosis.
The inflammatory cells of scleroma include:
a) Mikulicz cells: These are the pathognomonic cells. They are macrophages with clear (hydropic) cytoplasm and small central or eccentric nuclei (foamy macrophages).
b) Plasma cells and Russel bodies (hyalinized plasma cells).
c) Lymphocytes.

Complications
1-Nasal obstruction and deformity.
2-Ulceration, bleeding (epistaxis) and secondary bacterial infection



White Knightstone

SINUSITIS

This is inflammation of the mucosa of the paranasal sinuses. Commonly associated with rhinitis.

1-Acute Catarrhal & Allergic Sinusitis: Occur in association with similar types of acute rhinitis.

2-Chronic Sinusitis:

Aetiology:

- A complication of repeated attacks of acute rhinitis and sinusitis.
- Spread of infection from an infected tooth (mainly maxillary sinus).

Pathology:

- Chronic **nonspecific** sinusitis (chronic inflammatory cells, endarteritis & fibrosis)
- Nasal Sinus **Polyps:** Same as nasal polyps (describe, gross & microscopic picture & complications)
- Mucocele And Empyema Of The Maxillary Sinus:** Obstruction of the maxillary sinus ostium due to chronic sinusitis leads to retention of mucous discharge inside the sinus (mucocele). Secondary infection of the mucocele → accumulation of pus inside the sinus (empyema).

PHARYNGITIS

X 1-ACUTE PHARYNGITIS:

Aetiology: Commonly streptococcus hemolyticus infection

Pathology: Catarrhal or suppurative inflammation.

Complications:

- Spread of infection may lead to:
 - adenoids, laryngitis, otitis media, bronchitis, pneumonia...etc
 - cellulitis of neck
 - retropharyngeal abscess
- Development of autoimmune disease as rheumatic fever or glomerulonephritis

X 2-CHRONIC PHARYNGITIS: a) Nonspecific following acute pharyngitis b) Specific as scleroma

3-ADENOIDS

Definition: This is hyperplasia of the lymphoid tissue present at the posterior wall of the nasopharynx of infants and children due to chronic infection.

Pathology:

- Gross features:** Swollen adenoid tissue.
- Microscopic features:** Hyperplastic lymphoid follicles
- Effects:**
 - Nasopharyngeal obstruction** → mouth breathing. The child's face acquires characteristic features called **ADENOID FACE**, characterized by:
 - Open mouth.
 - Short upper lip.
 - Protruding upper central incisors
 - Narrow nasal openings
 - Absent nasolabial folds
 - Spread of infection → otitis media, bronchitis... etc.

4-DIPHTHERIA

Aetiology: This is infection of the URT with *Corynebacterium diphtheriae* and rarely conjunctiva, nose, ear, vulva, skin wound are affected. The disease mainly affects unimmunized children 2-5 years

Pathology: pseudomembranous inflammation (see general pathology, describe)

Complications:

- Asphyxia
- Severe toxemia that may lead to:
 - Acute heart failure (due to toxic myocarditis)
 - Paralysis of respiratory, laryngeal and extraocular muscles
 - Acute adrenal insufficiency due to adrenal necrosis & hemorrhage
 - Zenker's degeneration (hyaline necrosis of skeletal muscles as rectus abdominis).

TUMORS OF NOSE, SINUSES & NASOPHARYNX

	1-BENIGN	2-MALIGNANT
Epithelial:	a) Squamous cell papilloma & inverted papilloma b) Pleomorphic adenoma of minor salivary glands	a) Squamous cell carcinoma b) Salivary gland carcinoma
Mesenchymal:	a) Angioma & osteoma b) Others as fibroma, myxoma, chondroma, lipoma	a) Angiosarcoma, osteosarcoma b) Others as fibrosarcoma, lymphoma
Neuroectodermal:	Nasal Glioma, neurofibroma	Malignant melanoma

(B) NASOPHARYNGEAL FIBROMA (JUVENILE ANGIOFIBROMA)

An uncommon benign tumor of young boys arising from the periosteum.

Gross: noncapsulated grayish pink mass projecting into the nasopharynx.

Microscopy: angiofibroma (fibroma rich in capillaries).

Complications: epistaxis.

(A) NASOPHARYNGEAL CARCINOMA

Age: Common in 2 age groups: 1) Young individuals; 15-25 years. 2) Old individuals; 60-70 years

Predisposing Factor: Upper respiratory infections with Ebstein-Barr (EB) virus.

Pathology: Two main patterns:

- Squamous cell carcinoma.
- Undifferentiated carcinoma, commonly associated with dense lymphocytic infiltrate and is therefore sometimes termed "Lymphoepithelioma".

Prognosis:

- Tumor spread occurs by direct and lymphatic routes (and late by blood).
- Radiotherapy is the treatment of choice. It cures over 50% of cases (particularly young individuals).

(B) EPISTAXIS

Definition: Epistaxis means bleeding from the nose.

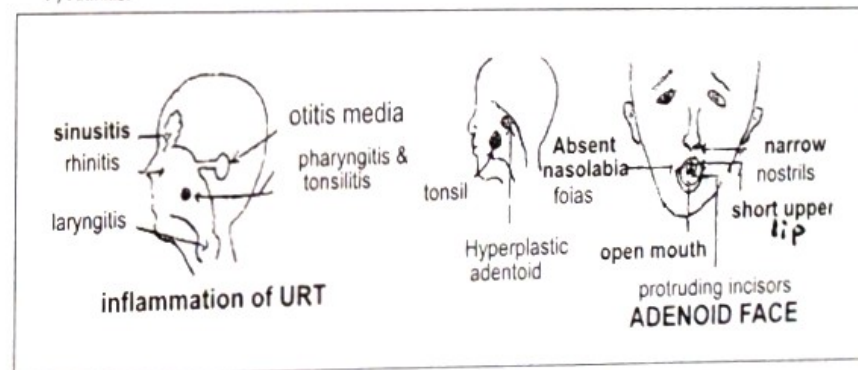
Aetiology:

1-Local Causes:

- Trauma.
- Foreign bodies
- Tumors (of nose & sinuses)
- Nasal polyp.
- Rhinoscleroma.
- Rhinitis.

2-General Causes:

- Hypertension.
- Fevers
- Hot climate
- Blood diseases as leukemia & purpura
- Vitamin C or K deficiency



DISEASES OF TONSILS & MIDDLE EAR

(A) ACUTE TONSILLITIS

AETIOLOGY:

Bacterial infection; most commonly streptococcus hemolyticus

PATHOLOGY: Three types:

- 1-Catarrhal Tonsillitis: Enlarged tonsils with hyperemic mucosa.
- 2-Follicular (suppurative) Tonsillitis: Remarkably enlarged tonsils. Lymphoid follicles show pus which appears at the tonsillar crypts.
- 3-Membranous Tonsillitis: In severe cases mucosal necrosis + exudate → a membrane covering the tonsils.

COMPLICATIONS:

- 1-Direct spread →
 - a) Peritonsillar abscess (Quinzy).
 - *b) Otitis media
 - c) Pharyngitis, laryngitis, bronchitis.
- 2-Lymphatic spread leads to cervical lymphadenitis.
- 3-Blood spread leads to bacteraemia, toxemia ...
- 4-Hypersensitivity reactions as:
 - a) Rheumatic fever.
 - b) Glomerulonephritis.
- 5-Chronic nonspecific tonsillitis.



(A) CHRONIC TONSILLITIS

Chronic Nonspecific Tonsillitis:

Characterized by hyperplasia of lymphoid follicles, chronic inflammation and fibrosis

Chronic Specific Tonsillitis as tuberculosis (see general pathology)

(A) ACUTE SUPPURATIVE OTITIS MEDIA

AETIOLOGY: Infection of the middle ear is due to spread of pyogenic bacteria through the Eustachian tube from nearby infections as tonsillitis, adenoids and pharyngitis.

PATHOLOGY:

- 1-The Eustachian tubes are obstructed due to inflammation and swelling of their mucosa.
- 2-The cavity of the middle ear is filled with pus.
- 3-Tympanic membrane bulges then perforates → purulent discharge from ear.

COMPLICATIONS:

- 1-Spread of infection →
 - a) Mastoiditis
 - b) Intracranial infections as lateral sinus thrombophlebitis, meningitis & brain abscess
- 2-Aural polyp: Mass of granulation tissue.
- 3-Chronic suppurative otitis media, this may lead to:
 - a) Tympanosclerosis
 - b) Cholesteatoma: This is ingrowth of abundant keratinizing squamous epithelium from the tympanic membrane into the lumen of the middle ear



DISEASES OF LARYNX

(C) LARYNGITIS

1-ACUTE LARYNGITIS:

Aetiology:

- 1-Bacterial infection; commonly streptococcus hemolyticus.
- 2-Viral infection e.g. measles.
- 3-Chemical irritation e.g. inhalation of irritant gases as chlorine and fumes.
- 4-Mechanical irritation faulty excessive use of voice → vocal cord irritation.

Pathology: Catarrhal inflammation (swollen hyperemic mucosa showing excess mucous).

2-CHRONIC LARYNGITIS:

- a) Nonspecific due to chronic irritation with smoking or chronic faulty use of voice. The vocal cords show chronic inflammation or laryngeal nodules (see below). Clinically hoarseness of voice.
- b) Specific as i) laryngoscleroma ii) tuberculous laryngitis iii) syphilitic laryngitis

(B) LARYNGEAL NODULE

(Laryngeal Polyp or Singer's Node)

It is a common lesion that occurs in the middle 1/3 of the true vocal cord. It is related to excessive use of the voice and occurs in singers (Singer's nodule) and teachers and is believed to be the result of trauma.

Grossly: it is a firm rounded nodule covered by mucosa.

Microscopically: it consists of dilated vascular spaces, fibrosis and myxomatous changes.

Clinically: the patient complains of hoarseness of voice.

TUMORS OF LARYNX

1-SQUAMOUS CELL PAPILLOMA OF LARYNX

May be induced by human papilloma virus. May occur in children (juvenile) or adults:

- 1-Papilloma of adults is more commonly solitary arising in a vocal cord, rarely multiple. Malignant change is rare. Excision is curable with no tendency for recurrence
- 2-Papilloma of children is more commonly multiple (papillomatosis) arising in and outside vocal cords. Malignant change is extremely occasional. Recurrence after excision is common.

exam ✓ 5P 2011

2-SQUAMOUS CELL CARCINOMA OF LARYNX

Cancer larynx is not uncommon (2% of all cancers of men). Usually occurs above the age of 40. Males are more common than females (ratio 7:1). Invasive cancer is commonly preceded by carcinoma in situ (75% of cases). Predisposing factors include smoking and papilloma.

PATHOLOGY:

Anatomical Site:

- 1-Glottic (65%): The tumor arises from the vocal cords (particularly the anterior third). These tumors present clinically with hoarseness of voice and can therefore be detected & treated early. Microscopically most of these tumors are well differentiated and therefore grow relatively slowly. For all of these reasons glottic tumors have the best prognosis.
- 2-Supraglottic (35%) and infraglottic (<5%): These tumors tend to be less differentiated and usually have less favorable prognosis than the glottic type.
- **Gross:** In most cases, the tumor appears as an ulcerated mass. Sometimes the tumor is very small and may be hardly visible grossly.
- **Microscopy:** Squamous cell carcinoma ranging between well and poorly differentiated.
- **Spread:** Direct and by lymphatics (to cervical nodes). Blood spread is late.

DISEASES OF THE LOWER RESPIRATORY SYSTEM

THE LOWER RESPIRATORY TRACT (LRT):

It consists of : 1) Trachea & bronchi 2) Lungs 3) Pleura
Diseases of the LRT are clinically referred to as diseases of the chest

DISEASES OF THE TRACHEA, BRONCHI & LUNGS

BRONCHIECTASIS (A) *دisease of bronchie*

DEFINITION: Persistent dilatation of medium-sized bronchi & bronchioles, accompanied by chronic suppurative inflammation of their walls.

AETIOLOGY AND PATHOGENESIS:

1-Septic Bronchopneumonia: Particularly in children. Mechanism of bronchiectasis:

- The inflamed bronchial walls are weak → easily pulled by the negative intrathoracic pressure.
- Interference with the cough reflex → retention of the exudate within the bronchial lumens.
- The adjacent inflamed alveoli may become fibrotic → pull on the bronchial walls.

2-Bronchial obstruction: Long standing obstruction by foreign bodies, tumors...etc leads to:

- Bronchial obstruction predisposes to infection (septic bronchopneumonia) → see above.
- Obstruction → collapse of alveoli → exaggeration of the negative intrathoracic pressure → exaggerated pull on the bronchial walls.

3-Congenital lesions:

a) Kartegener's syndrome: It consists of situs inversus, sinusitis & bronchiectasis. The later is due to defective ciliary motility → defective clearance of bacteria → infection → bronchiectasis

b) Mucoviscidosis: A congenital disease characterized by thick mucous secretions → bronchial obstruction & infection → bronchiectasis. = *NaCl ↑* *والتست*

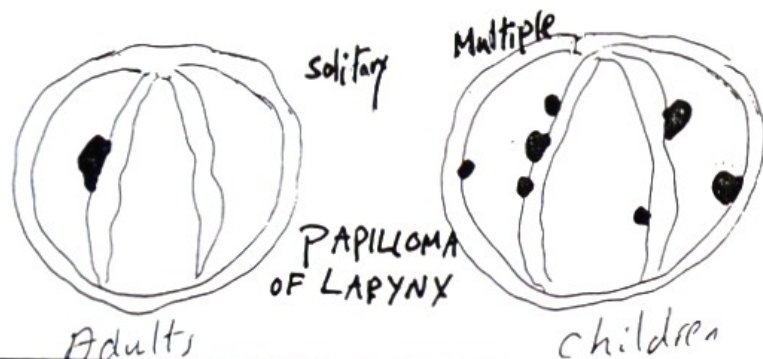
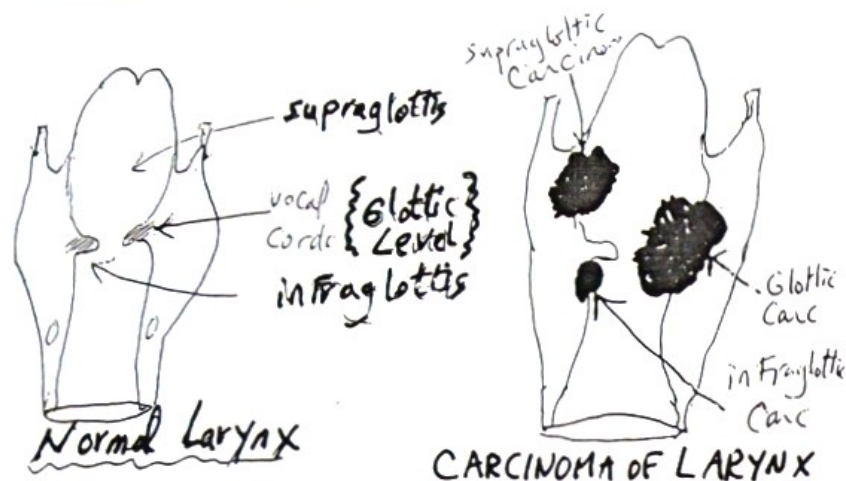
Pathogenesis:

GROSS:

- Usually bilateral. *site*
- More common in lower lobes
- It has a patchy distribution.
- Bronchial dilatation may be cylindrical, fusiform or saccular. *1b*
- An important diagnostic feature is the finding of enlarged dilated bronchi near the pleura (due to their exaggerated dimensions).
- Lumen contains pus, mucus and blood.
- Mucosa shows ulcerations.
- Surrounding alveoli are fibrotic.
- Covering pleura shows pleurisy then fibrosis.
- The draining lymph nodes are enlarged.

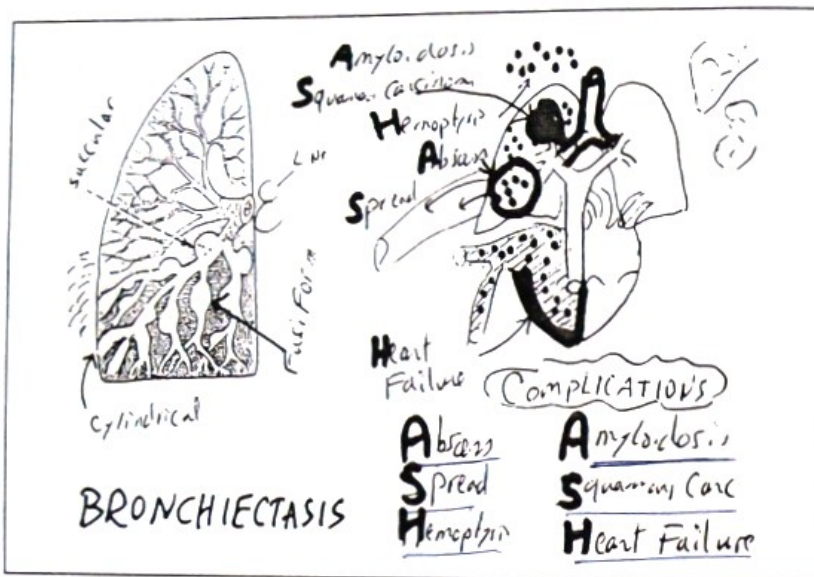
MICROSCOPY: Bronchi are dilated and show:

- Lumen: Shed epithelial cells, inflammatory cells and erythrocytes.
- Mucosa: Ulcerations, squamous metaplasia.
- Rest of bronchial wall: Destruction of musculoelastic tissue, fibrosis and inflammatory cells (neutrophils, macrophages, lymphocytes & plasma cells).
- Adjacent lung and pleura: Inflammatory cells, fibrosis.



= Septic pneumonia = Lung Abscess

- 1-Haemoptysis
- 2-Lung abscess which may be complicated by gangrene.
- 3-Direct spread (empyema , pericarditis mediastinitis).
- 4-Blood spread (septic thrombophlebitis , pyaemia...etc).
- 5-Secondary amyloidosis. ***
- 6-Lung fibrosis which may lead to right sided heart failure.
- 7-Squamous carcinoma on top of squamous metaplasia.



Aetiology:

- 1-Viral infections as influenza.
- 2-Bacterial infections as pneumococci
- 2-Hypersensitivity
- 4-Chemical irritants as fumes.

Pathology: Catarrhal inflammation (see general pathology).

منظري وید (A) VSP Jar slide (COPD) منس عارف - صحیح الجواب

COPD group is characterized by an increase in resistance to air flow due to partial or complete obstruction at any level. The most important obstructive disorders (excluding tumors and foreign bodies) are: 1-Bronchial asthma, 2-chronic bronchitis, 3-Emphysema.

Complication
التهاب الرئة
+
emphysema

Partial only, $\mu_{\text{is}} / 2$ not complete

Types only

episodic not permanent

DEFINITION: Asthma is a type of COPD characterized by episodes of reversible bronchospasm resulting from increased responsiveness of the bronchial tree to various stimuli.

AETIOLOGICAL TYPES OF BRONCHIAL ASTHMA:

1-Extrinsic Asthma:

- It is an atopic disease (type I hypersensitivity). Repeated exposure to committed antigens a pollens, house dust & fungi → mast cell release of important mediators as histamine, leukotrienes, prostaglandins & platelet activating factor leading to:
 - a) bronchospasm
 - b) increased vascular permeability → bronchial mucosal oedema
 - c) increased mucin secretion and accumulation of eosinophils.
- Extrinsic asthma starts in children and young adults.
- As in other atopic diseases, hereditary predisposition is common.

2-Intrinsic Asthma:

- May be caused by pulmonary infections ; particularly viral. Intrinsic asthma may be also induced by drugs (as aspirin), cold, psychological stress & inhaled irritants.
- It usually develops in middle -aged and elderly adults.

PATHOLOGICAL FEATURES:

Gross picture: During the attacks:

- There is spasm of the small bronchi and bronchioles which appear narrowed & thickened due to oedema, associated with excessive mucin secretion appearing as intralumen mucous plugs.
 - The lungs are over-inflated: Explanation:
 - Normally during inspiration the bronchi become wider allowing air entry, while during expiration they become narrower.
 - In case of bronchial asthma, bronchial dilatation during inspiration will allow air entry. On the other hand, Bronchospasm & mucin. Secretion will aggravate the expiratory bronchial narrowing → much trapping of air.
- N.B: dyspnea of asthmatic patients is expiratory more than inspiratory

Microscopic picture:

- 1-Narrowing of the small bronchi and bronchioles.
- 2-Bronchial mucosa and submucosa shows oedema & inflammatory cells particularly eosinophils.
- 3-The bronchial lumens are plugged with mucus containing spirals of shed epithelium (Curschmann's spirals) and eosinophils.
- 4-By time, there is hyperplasia of mucosal glands and hypertrophy of bronchial muscle.

COMPLICATIONS :

- 1-Secondary infection and chronic bronchitis .
- 2-Chronic bronchitis predisposes to emphysema.

→ persistent

* clinical def. key in context

Definition: Chronic bronchitis is defined as persistent productive cough for at least 3 consecutive months in at least 2 consecutive years.

Aetiology:

1-Predisposing Factors:

- a) It is common among cigarette smokers.
- b) Bronchial asthma.
- c) Chronic upper respiratory infection as sinusitis
- d) Chronic lung disease as chronic venous congestion
- e) It may follow repeated attacks of acute bronchitis.

2-Causative organisms: Pneumococci, *H. influenzae* & others.

صالح بن عبد الله المحمدي
ابن محمد بن علي
بالحركة للكتاب في شهر المحرم
السنة ١٢٠٥ هـ

Gross Picture:

- 1-Swollen congested mucosa.
- 2-Thickened bronchial walls

Microscopic Picture:

- 1-Mucosal hyperplasia & squamous metaplasia. Mucosal atrophy may occur late.
- 2-Chronic inflammatory cells and fibrosis affecting the bronchial walls.

Types of Chronic bronchitis:

- "simple chronic bronchitis" characterized by mucoid sputum.
- "chronic mucopurulent bronchitis" characterized by mucoid sputum mixed with pus
- "chronic asthmatic bronchitis" which clinically resembles atopic bronchial asthma.

EMPHYSEMA (A)

DEFINITION: This permanent over-distension of the air spaces distal to the terminal bronchioles accompanied by destruction of their walls.

PATHOGENESIS:**1-Excessive Protease (Elastase) Activity:**

- Excess protease activity → destruction of the elastic tissue of the air spaces → diminished elastic recoil → progressive distension of the air spaces.
- The main sources of protease are the **neutrophils & macrophages**.
- Excess protease activity occurs in the following conditions:
 - a) **Congenital deficiency of protease inhibitor** (alpha 1 antitrypsin deficiency, " $\alpha 1$ -AT" deficiency) → unopposed action of protease.
 - b) **Cigarette Smoking:** see below

2-Cigarette smoking:

- Smokers have greater numbers of neutrophils and macrophages in their bronchi.
- Smoking stimulates the release of elastase from neutrophils.
- Smoking enhances elastase activity in macrophages.
- Oxidants in cigarette smoke inhibit $\alpha 1$ -AT.
- Smoking leads to chronic bronchitis.

3-Chronic bronchitis is a helping factor due to:

- Swelling of the inflamed bronchial mucosa → partial bronchial obstruction.
- Exaggerated obstruction during expiration → trapping of much air.

REMARK: Emphysema is a type of COPD. Bronchial obstruction is always present due to:

- 1) Chronic bronchitis which is an aetiological factor.
- 2) Compression of the bronchi by the distended emphysematous air spaces.

TYPES OF EMPHYSEMA:**1-CENTRIACINAR (Centrilobular or Bronchiolar) EMPHYSEMA:**

- **Definition of respiratory acinus:** The acinus is the part of the lung distal to the terminal bronchioles & consists of respiratory bronchioles followed by alveolar ducts and alveoli.
- A cluster of 3-5 acini is referred to as lobule.
- **Definition of centriacinar emphysema:** A type of emphysema in which respiratory distension affects the central (proximal) part of the respiratory acini, i.e. the respiratory bronchioles. The alveoli are spared.
- Centriacinar emphysema is the main type seen in smokers.
- It may progress to panacinar emphysema.

2-PANACINAR (Panlobular or Alveolar) EMPHYSEMA:

- Distension affects all parts of the acinus (respiratory bronchioles, alveolar ducts & alveoli).
- It is the main type occurring in cases of $\alpha 1$ -AT deficiency.

MICROSCOPY:

- 1-Distension affects:

* **Complication**
= **Bronchial Asthma**
② **emphysema**

*** Microscopy: slide**

- The respiratory bronchioles (in cases of centrilobular emphysema)
- The respiratory bronchioles, alveolar ducts and alveoli (in cases of panacinar emphysema).
- 2-The pulmonary capillaries are compressed.
- 3-Elastic tissue stains show reduced elastic tissue.
- 4-Walls of the affected spaces are thinned. In advanced cases, adjacent alveoli become confluent creating large air spaces.

*** GROSS FEATURES:****1-BOTH LUNGS:**

- Lungs are voluminous.
- They cover the heart and press the diaphragm.
- They do not collapse on opening the chest.
- They are dry, pale and light.
- The surface shows indentations at the sites of ribs
- Bullae (measuring few centimeters) may develop.

2-THE CHEST WALL:

- Barrel shaped chest (exaggerated inspiratory position) due to over-distension of lungs.
- Ribs become horizontal and subcostal angle is widened.

*** EFFECTS & COMPLICATIONS:**

- Chest wall deformity (barrel-shaped)
- Right sided heart failure (cor pulmonale) due to pulmonary hypertension.
- Respiratory failure. It leads to acidosis and cyanosis.
- Rupture of widened air spaces → pneumothorax or interstitial (mediastinal) emphysema.

OTHER TYPES OF EMPHYSEMA UNRELATED TO COPD: (X)**1-Paraseptal emphysema**

- Affects air spaces adjacent to septa or pleura i.e. the periphery of the respiratory lobules
- It may result from forces pulling on the septa e.g. fibroinflammatory lesions & atelectasis.
- It is a common cause of spontaneous pneumothorax in young adults

2-Irregular emphysema

- This is permanent enlargement of air spaces distal to terminal bronchioles, seen adjacent to lung scars (due to healed inflammatory lesions).
- It is a common type of emphysema, but does not affect the pulmonary functions.

3-Compensatory emphysema:

- If one lung is out of function (e.g. pneumonectomy or total collapse), the other lung shows compensatory over-distension of the air spaces.
- If parts of a lung are out of function (as in pneumonia), other parts in the same lung show compensatory over-distension.

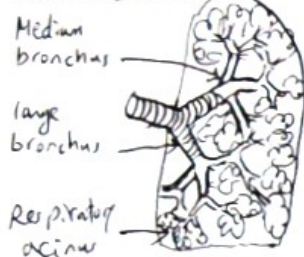
4-Senile (atrophic) emphysema:

This is senile hyperinflation of the lungs due to atrophy of the alveolar walls.

INTERSTITIAL (MEDIASTINAL) EMPHYSEMA:

- This is the presence of air outside the respiratory spaces, i.e. in the interstitial tissue of the lung, from which it escapes to the mediastinum.
- It may be due to severe coughing or trauma.
- Recovery is common (air is absorbed).
- Death may occur in severe cases due to compression of vessels.

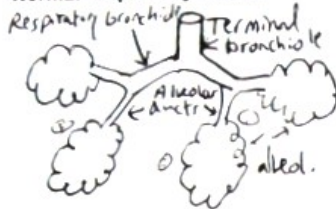
Normal lung Structure



PANACINAR EMPHYSEMA



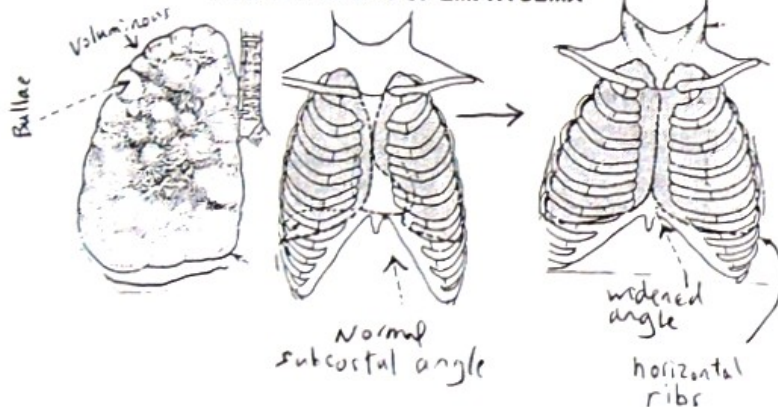
Normal respiratory acinus



CENTRIOLOBULAR EMPHYSEMA



GROSS FEATURES OF EMPHYSEMA



LUNG ABSCESS (A)

DEFINITION: A cavity containing pus due to localized suppurative inflammation of lung.

AETIOLOGY:

- Causative Bacteria:** Staphylococci, Pneumococci, or other pyogenic bacteria.

Conditions leading to lung abscess:

- Inhalation (aspiration) of septic material as:**
 - blood clots during surgical operations of upper respiratory tract.
 - vomitus in persons under general anesthesia.
 - foreign bodies...etc.
- Septic emboli** derived from septic thrombophlebitis → pyemic abscesses
- Bacterial pneumonia** (lobar pneumonia or bronchopneumonia) → post pneumonic abscess
- Bronchiectasis.**
- Bronchial obstruction** → accumulation of mucus → secondary bacterial infection
- Direct spread of septic infection** e.g. from subphrenic abscess.
- Secondary bacterial infection of hydatid cyst.**
- Bacterial infection following penetrating chest injuries.**
- Pulmonary actinomycosis** (see general pathology)

PATHOLOGY:

1-Inhalation (Aspiration) Lung Abscess:

Definition: Lung abscess caused by inhalation (aspiration) of septic material (describe).

Pathology: the right lung is more commonly affected: *mostly middle lobe*

- The abscess is usually single
- It is related to a peripheral bronchus.
- It appears as a variable-sized irregular cavity containing pus.
- The covering pleura shows pleurisy.
- Hilar lymph nodes are enlarged.
- Fibrosis replaces the abscess if small and surrounds it if large (chronic abscess).

2-Post-pneumonic Lung Abscess:

Definition: Lung abscess complicating bacterial pneumonia (lobar or septic bronchopneumonia)

Pathology: Single or multiple abscesses complicating pneumonia.

3-Pyemic Lung Abscesses:

Definition: Lung abscesses caused by septic emboli.

Pathology: Multiple bilateral small peripheral abscesses related to vessels.

COMPLICATIONS OF LUNG ABSCESS:

1-Rupture leads to:

- Hemoptysis
- Bronchopleural fistula and pyopneumothorax.

2-Lung Gangrene

3-Direct spread:

Empyema, pericarditis, mediastinitis.

4-Blood spread:

Septicaemia, pyaemia, meningitis, brain abscess.

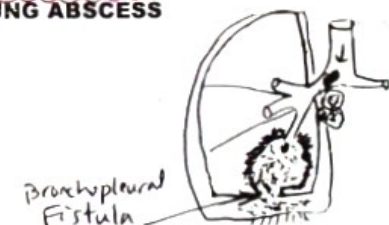
5-Chronic abscess may be complicated by:

secondary amyloidosis.

ASPIRATION LUNG ABSCESS

Complications

- Gangrene
- Rupture
- Amyloidosis (in case of chronicity)
- Spread by direct route
- Spread by blood



* why pleurisy } not too suffic = $\frac{2}{3}$ of the time
 * why pneumonia }
 * I have no chronic pneumonia only acute
 * Compensated + Jar + VJP + A PNEUMONIA

Definition: This is patchy or diffuse inflammation of the lung with consolidation.
Classification:
 • **Bacterial** as lobar pneumonia, septic bronchopneumonia, tuberculous & syphilitic pneumonia
 • **Non-bacterial** as viral pneumonia, parasitic (verminous) pneumonia, fungal pneumonia, allergic pneumonia, chemical & lipid pneumonia

مرض اليوم التاسع (9th day) Bacterial LOBAR PNEUMONIA VJP + Jar + 2 slide + Case + Compensated with septic

This is acute diffuse fibrinous inflammation of one or more lung lobes.

AETIOLOGY:

- 1-Predisposing factors a) Low resistance, b) Age: Young adults and middle aged persons
- 2-The causative bacteria: Pneumococci
- 3-Route of infection: Droplet infection.

PATHOLOGY: Four stages:

STAGE OF CONGESTION	STAGE OF RED HEPATIZATION	STAGE OF GRAY HEPATIZATION	STAGE OF RESOLUTION
DURATION: 1st day of illness	2nd-4th day	5th-8th day	9th day till day 21.
GROSS: The affected lobe appears: 1-Enlarged. 2-Red. 3-Consistency: Wet sponge. 4-Cut section exudes frothy fluid.	1-Enlarged. 2-Red. 3-Consolidated (hepatized). 4-Cut section: Dry. 5-Pleurisy. 6-Enlarged hilar lymph nodes.	1-Enlarged. 2-Gray. 3-Consolidated (hepatized). 4-Cut section: Dry. 5-Pleurisy. 6-Enlarged hilar lymph nodes.	Absence of necrosis → resolution is expected: 1-Fibrin is liquefied by proteolytic enzymes of dead neutrophils 2-Phagocytosis by macrophages 3-lymphatic drainage of the liquefied exudate → gradually restore the normal aeration of the alveoli. The lung will thus return to normal except that healing of pleurisy may lead to some adhesions.
MICROSCOPY: 1-Alveolar capillaries are congested. 2-Alveolar walls: Thickened. 3-Alveolar spaces: a) Bacteria. b) Fluid exudate.	1-Alveolar capillaries are congested. 2-Alveolar walls: Thickened. 3-Alveolar spaces: a) Bacteria. b) Fibrin. c) RBCs. d) Neutrophils.	1-Alveolar capillary congestion is reduced. 2-Alveolar walls: Thinned. Why? due to marked distention of alveoli → alveolar wall compression 3-Alveolar spaces show a) Dead bacteria. b) Fibrin shrinks. c) Hemolysed RBCs. d) Much neutrophils e) Macrophages	

CLINICAL COURSE:

- 1-The patient complains of fever, dyspnea, cough and chest pain.
- 2-At about the 9th day, the disease ends by **Crisis** (sudden improvement). However death may occur due to severe toxemia causing acute heart failure.

COMPLICATIONS:

- 1-Failure of resolution leading to fibrosis (carnification).
- 2-Toxaemia: toxic myocarditis (leading to heart failure). This occurs at about the 9th day when resolution starts where bacterial toxins become absorbed.
- 3-Direct spread: empyema (pus in pleural sac), pericarditis, mediastinitis.
- 4-Blood spread: septicaemia, meningitis, osteomyelitis
- 5-Post-pneumonic lung abscess and gangrene.

VJP + Jar + Case + Compensated Patchy not diffuse
 Bacterial SEPTIC BRONCHOPNEUMONIA = Lobular pneumonia
Definition: Bronchopneumonia (lobular pneumonia) is patchy inflammation of bronchioles & adjacent alveoli.
AETIOLOGY:
 The causative bacteria: Staphylococci, Streptococci, Pneumococci, Haemophilus influenzae.
 Route of infection:
 a) Endogenous from upper respiratory tract.
 b) Exogenous (droplet infection).
 Predisposing factors:
 a) Extremes of age (young and old).
 b) Low resistance as in diabetes and cachexia.
 c) Bronchitis.
 Gross: Both lungs particularly lower lobes show:
 1-Multiple consolidated yellowish patches exuding pus on pressure.
 Several patches may coalesce (confluent bronchopneumonia).
 2-Fibrinous pleurisy and enlarged hilar lymph nodes.

AETIOLOGY:

- 1-The causative bacteria: Staphylococci, Streptococci, Pneumococci, Haemophilus influenzae.
- 2-Route of infection:
 a) Endogenous from upper respiratory tract.
 b) Exogenous (droplet infection).
- 3-Predisposing factors:
 a) Extremes of age (young and old).
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 c) Bronchitis.

GROSS: Both lungs particularly lower lobes show:

- 1-Multiple consolidated yellowish patches exuding pus on pressure.
 Several patches may coalesce (confluent bronchopneumonia).
- 2-Fibrinous pleurisy and enlarged hilar lymph nodes.

MICROSCOPY:

- 1-Wall of affected bronchioles shows congested capillaries, neutrophils, & pus cells. Some of these inflammatory cells appear in the lumen.
- 2-The adjacent alveoli show 3 successive zones:
 a) Alveolar inflammation (capillary congestion, neutrophils, pus cells, fibrin).
 b) Alveolar collapse.
 c) Alveolar dilatation (compensatory emphysema).

COMPLICATIONS:

- 1-Fibrosis.
- 2-Toxaemia: toxic myocarditis.
- 3-Direct spread: empyema, pericarditis, mediastinitis.
- 4-Blood spread: septicaemia, meningitis...
- 5-Post-pneumonic lung abscess and gangrene.
- 6-Bronchiectasis.

INTERSTITIAL & VIRAL PNEUMONIA

Definition: Interstitial pneumonia is lung inflammation in which the inflammatory infiltrate is predominantly interalveolar (interstitial). Commonly viral, less commonly otherwise.

Aetiology:

- 1-Viral infections
 a) Primary respiratory involvement as influenza
 b) Secondary respiratory involvement as in measles, herpes & CMV
- 2-Other infections as mycoplasma & pneumocystitis carinii
- 3-Chemicals & drugs as cyclophosphamide, heroin, barbitone
- 5-Physical irritation as fumes of burns

Pathology:

A) Mild Cases:

The common type of viral interstitial pneumonia is characterized by: Grossly bilateral peribronchial congested patches and fibrinous pleurisy.

Microscopically: interstitial inflammation characterized by congested capillaries, oedema, lymphocytes, plasma cells & macrophages. The alveoli are compressed but no alveolar necrosis.

Fate & complications:

- 1-Resolution is common.
- 2-Development of interstitial fibrosis is uncommon.
- 3-Secondary bacterial infection → septic bronchopneumonia.

لو او نه و لغت
 4% die bec heart
 80% pneumonia

No Consolidation

White bright dots

* نوع عالم اشهر لم يجر كثيرا جملنا مريضا اذ مثل انفلونزا
 46
 47

B) Severe Cases: Adult Respiratory Distress Syndrome (ARDS):

- 1-In the early stage (exudative phase) the disease is characterized by diffuse alveolar damage (DAD) manifested by necrosis, fibrin deposition, hyperplasia of alveolar cells (pneumocytes) and inflammatory cells (lymphocytes, plasma cells & macrophages).
- 2-In surviving patients, repair occurs (proliferative phase) ending in interstitial fibrosis (fibrous phase) which leads to microcystic changes (honeycomb lung).

Complications of ARDS: Death due to respiratory failure.

INFLUENZA

VIP+
 CIP

كيس مري
 viral pneumonia

Definition & Aetiology: A common respiratory droplet infection caused by one of many types of influenza viruses (mainly types A, B & C). Incubation period is short (1-2 days).

Pathological Features:

1-Upper respiratory tract lesions: Catarrhal rhinitis, sinusitis, nasopharyngitis & laryngitis.

Grossly: The mucosa is oedematous, hyperemic & swollen.

Microscopically:

- a) Mucoid degeneration and shedding of mucosal epithelial cells.
- b) Submucosa shows congested capillaries, oedema, lymphocytes, plasma cells & macrophages.

2-Bronchi: Bronchitis. Gross & microscopic picture: similar to upper respiratory tract lesions

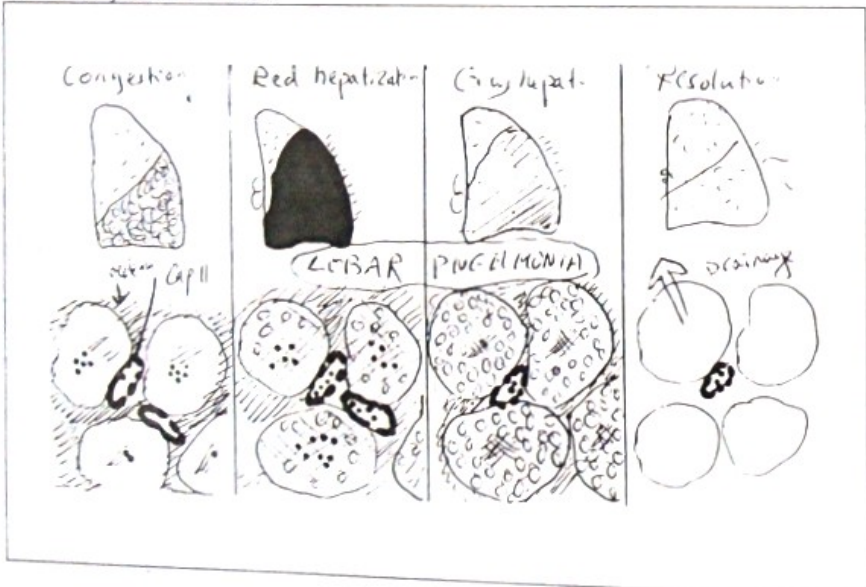
3-Lungs: Interstitial bronchopneumonia. Grossly by bilateral peribronchial congested patches.

Microscopically interstitial inflammation without alveolar necrosis (congestion, oedema, lymphocytes, plasma cells, macrophages)

Fate & Complications:

- 1-Influenza commonly resolves without complications.
- 2-Secondary bacterial infection.

ARDS شرح



LUNG GANGRENE (X)

Definition: An infective gangrene complicating suppurative lung infections.

Aetiology:

1-Severe lung infections as lung abscess, bacterial pneumonia and bronchiectasis. Necrosis caused by bacterial toxins ± inflammatory thrombosis of arteries may be followed by putrefaction → gangrene.

2-Putrefaction: by saprophytes of the respiratory tract (as fusispirochaetae organisms).

Pathology:

- 1-The gangrenous area appears black, friable and foul smelling.
- 2-The vessels are destroyed leading to severe hemoptysis
- 3-Death results from a) severe hemoptysis b) severe toxemia.

REMARK: SUPPURATIVE LUNG DISEASES include:

- 1) Lung abscess
- 2) Bronchiectasis
- 3) Septic bronchopneumonia
- 4) Empyema

PNEUMOCONIOSIS (B)

DEFINITION: This is a group of chronic lung diseases caused by inhalation of dust particles as carbon, silica, cotton fibers, bagasse, asbestos, beryllium, cement...etc.

TYPES:

1-Silicosis: It is due to inhalation of silica particles (as in miners) leading to granulomas:

Gross: Both lungs show numerous hard small grayish nodules.

Microscopy: Multiple foreign body granulomas composed of silica particles, surrounded by macrophages, foreign body giant cells, lymphocytes & fibrosis.

Complications:

- 1) Pulmonary fibrosis which may → right sided heart failure (cor pulmonale)
- 2) Bronchogenic carcinoma
- 3) Pulmonary tuberculosis is common due to lowered lung resistance.

2-Byssinosis: Inhalation of cotton fibers → lung fibrosis.

3-Bagassosis: Inhalation of cane sugar fibers → lung fibrosis.

4-Asbestosis: Inhalation of asbestos →

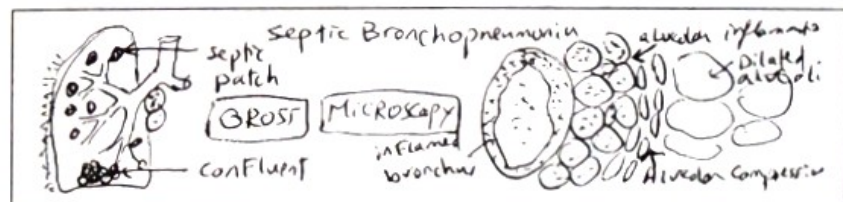
- Lung fibrosis
- Pleural mesothelioma is common.

5-Anthracosis: Inhalation of carbon particles (mildest form of pneumoconiosis).

Gross: Both lungs show black patches

Microscopy: Macrophages engulf these particles and carry them to the draining lymph nodes, which together with the affected lungs appear black.

Complications are rare. Fibrosis does not occur (except rarely in severe cases e.g. in coal miners).



الانسبوسيس
 هو مرض مزمن في الرئة
 يحدث نتيجة استنشاق
 الغبار أو الألياف
 الدقيقة مثل السيليكا
 أو الكربون أو القطن
 أو قصب السكر (الباغاسا)
 أو الصوف (البيسينوسيس)
 أو الأسبستوس (الاستبوسيس)
 حيث تدخل هذه الجسيمات
 الصغيرة في الرئة وتتراكم
 في الحويصلات الهوائية
 مسببة التهابات مزمنة
 وتندب الرئة مع مرور
 الزمن مما يقلل من قدرتها
 على التنفس.

GRANULOMATOUS LUNG DISEASES X

- 1) Tuberculosis
- 2) Sarcoidosis
- 3) Pneumoconiosis
- 4) Fungal infections as histoplasmosis
- 5) Parasitic disease as bilharziasis
- 6) Others as actinomycosis, syphilis

PULMONARY OEDEMA X

A) ACUTE PULMONARY OEDEMA:

Aetiology:

- 1- Acute left sided heart failure
- 2- inhalation of irritant gases
- 3- severe viral pneumonia
- 4- rapid withdrawal of massive pleural effusions
- 5- Increased intracranial tension

Gross Features: The lungs are heavy, pale and ooze frothy fluid on pressure.

Microscopy: Interstitial and intra-alveolar pale pink fluid.

Complications:

- 1- Asphyxia
- 2- secondary bacterial infection.

B) CHRONIC PULMONARY OEDEMA:

Aetiology:

- 1- Chronic lung congestion as in chronic left ventricular failure
- 2- As a part of generalized oedema.

Gross & Microscopy: As acute pulmonary oedema.

Complication: Secondary bacterial infection

RESTRICTIVE LUNG DISEASES B

Restrictive lung diseases are characterized by stiff lungs (reduced lung compliance), i.e. more pressure is required to expand the lungs. Restrictive lung diseases include:

- 1- Acute disease as adult respiratory distress syndrome (ARDS). See interstitial pneumonia.
- 2- Chronic disease as diffuse interstitial pulmonary fibrosis:
 - Causes: a) idiopathic b) Collagen diseases as SLE c) Pneumoconiosis & others.
 - Pathology: Progressive interstitial/ alveolar septal fibrosis. The end stage is characterized by wide cystic spaces (honey comb lung) → respiratory failure.

LUNG ATELECTASIS B MCQ + anal

Definition: This is inadequate expansion of the air spaces (atelectasis) in the new born.

Types, Aetiology & Pathology:

1- Complete (total) atelectasis

- Non-expansion of the lungs may be due to cerebral birth injuries or intrauterine hypoxia.
- The baby is born dead (stillbirth).
- **Grossly** the lungs are fleshy (do not crepitate under pressure as observed in normal lungs) & blue (non-oxygenated blood).
- **Microscopically** slit-like alveoli.

2- Incomplete (partial) atelectasis: It is due to hyaline membrane disease:

- Hyaline membrane disease is more common in premature infants, particularly those born by caesarian section and in case of maternal diabetes mellitus.
- **Grossly** the lungs are fleshy and purple-red.
- **Microscopically** the bronchioles, alveolar ducts and random alveoli are lined by a thick eosinophilic membrane composed of necrotic cells and fibrin.
- The condition may be fatal, but treatment with synthetic surfactants have reduced the mortality and nowadays 85-90% of these infants survive when treated.

(B) LUNG COLLAPSE

Definition: This is acquired deflation of the lung; all or part.

Types, Aetiology & Pathology:

1- Absorption (Obstructive) Collapse:

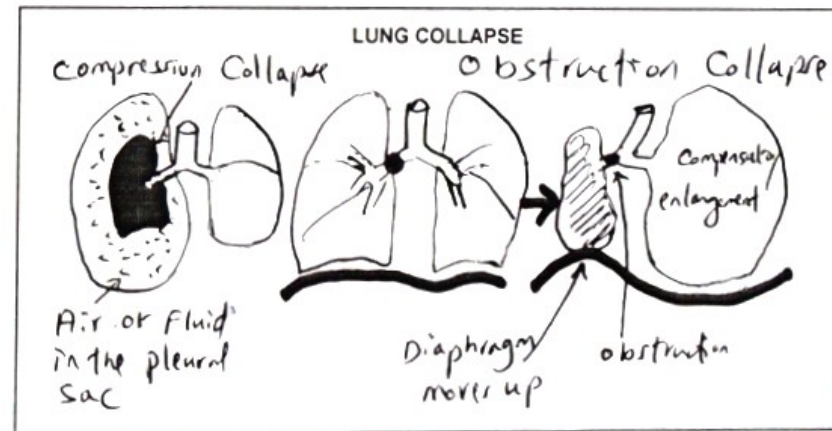
- **Causes:** Complete bronchial obstruction → collapse due to gradual absorption of trapped air. Bronchial obstruction may be:
 - **Endogenous:** Bronchial lumen obstruction by foreign bodies, mucus plugs, tumors, clots
 - **Exogenous:** Compression of the bronchi by enlarged nodes or tumors.

• Pathology:

- Lung collapse may be total if the hilar bronchus is obstructed. In these cases the chest wall retracts opposite the affected lung, the diaphragm moves upwards at the affected side and the mediastinal structures shift towards the collapsed lung.
- More commonly lung collapse is lobar or lobular (if a small bronchus is obstructed).
- The collapsed part appears bluish, rubbery and does not crepitate.
- Microscopically: Narrow alveolar lumens & dilated interalveolar capillaries.

2- Compression (Pressure) Collapse:

- **Causes:** Pressure on lung may be:
 - **Endogenous** intrapleural causes as pneumothorax, hydrothorax, chylothorax, hemothorax or empyema.
 - **Exogenous:** Pressure on lungs by elevated diaphragm (as in case of ascites), by pericardial effusion or by enlarged dilated heart.
- **Pathology:** Compression collapse may be:
 - Massive as in cases of pneumothorax.
 - Basal (commonly bilateral) e.g. due to elevated diaphragm or massive pleural effusions.



Oral
* Squamous Cell carcinoma doesn't become malign only in Lung bec. oral origin
(A) TUMORS OF THE LUNG

BENIGN TUMORS:

- 1-Epithelial as bronchial papilloma
- 2-Mesenchymal as chondroma, fibroma, angioma, lipoma, hamartoma.

PRIMARY MALIGNANT TUMORS:

1-Epithelial

- a-Bronchogenic carcinoma
- b-Bronchioloalveolar carcinoma.
- c-Others as adenoid cystic carcinoma

2-Mesenchymal as chondrosarcoma, Fibrosarcoma, leiomyosarcoma

3-Embryonic: Pulmonary blastoma

4-Primary lung lymphoma

LOCALLY MALIGNANT TUMORS: Bronchial carcinoid.

SECONDARY (METASTATIC) TUMORS: Derived from

- 1-Carcinomas
- 2-Sarcomas
- 3-Lymphoma & leukemia
- 4-Malignant melanoma

Cells are

BRONCHIAL CARCINOID (A)

Locally Malignant

GIT Carcinoid Case

DEFINITION:

- A low grade malignant tumor that arises from neuroendocrine cells of the bronchial mucosa.
- Most carcinoids have a locally malignant behaviour
- Most cases are resectable & curable.
- A malignant metastasizing behaviour may uncommonly occur.

Def: Locally malign neoplasm arising from neuroendocrine cells

AGE & SEX:

- Young and older persons with a median age of 40 years.
- Both sexes are equally affected.

GROSS:

- A spherical mass, usually less than 4 cm in diameter, usually covered by intact mucosa
- The mass projects into the bronchial lumen
- It may infiltrate the lung tissue & appear dumb-bell shaped

MICROSCOPY:

- Masses of uniform small cuboid cells with regular nuclei
- Unremarkable mitosis and no necrosis
- The cells contain argyrophilic granules that can be shown by silver stains.

EFFECTS:

- Bronchial obstruction.
- Hemoptysis.
- Carcinoid syndrome.
- Nodal metastases (6-9%) & distant metastases (5%).

Remark: Atypical Carcinoid tumor is the term given to more aggressive carcinoids characterized by mitoses & tumor necrosis. Up to 70% of these tumors metastasize.

BRONCHOGENIC CARCINOMA

More common in males. Mainly above age of 40 years.

PREDISPOSING FACTORS:

- Tobacco smoking (aromatic hydrocarbons & phenol derivatives)

Def: A malign. neoplasm arising from epith of Bronchus
Aetiology - age - sex + predisposing factors

VIP + J₂ + Case + squamous Carcin

- Air pollution with exhaust fumes of tar and diesel.
- Silicosis asbestosis & industrial chemicals as arsenic & nickel
- Bronchiectasis
- Lung scarring.
- Irradiation
- Genetic factors.

GROSS PICTURE:

1-Central (Hilar) Type (85%):

- It arises from the main bronchi
- It forms a polypoid, ulcerative or infiltrative growth patterns with necrosis & hemorrhage.
- Bronchial destruction & lung invasion occurs.

2-Peripheral Type (15%):

- It rises from the peripheral bronchi
- It appears as single or multiple nodular growths at the peripheral aspects of the lung.

MICROSCOPY: Any of the following type:

1-Squamous cell carcinoma: Commonest

- It is the commonest type.
- It arises from the main bronchi.
- It is usual type in carcinoma arising in smokers.
- It is usually poorly differentiated.

2-Anaplastic carcinoma small cell type (Oat Cell Carcinoma):

- It is the second most common type of primary lung cancer and is related to smoking
- It arises from neuroendocrine cells
- It occurs in central portions of the lung.
- It consists of small round or oval cells having dark nuclei showing high mitotic activity & extensive necrosis.
- Paraneoplastic syndromes (as Cushing syndrome & carcinoid syndrome) may occur.

3-Anaplastic carcinoma large cell type or giant cell type.

4-Adenocarcinoma:

- More common in females (50% of lung cancer in females) (Not related to smoking. !!!)
- Uncommon in males.
- Occurs mainly at lung periphery.

5-Adenosquamous carcinoma: rare.

SPREAD:

- 1-Direct within the lung, to pleura and mediastinum.
- 2-Lymphatic to hilar, mediastinal and supraclavicular lymph nodes.
- 3-Blood spread:
 - Through pulmonary artery → metastases in lungs.
 - Through pulmonary veins → metastases liver, brain, bones...

OTHER EFFECTS OF BRONCHOGENIC CARCINOMA:

- 1-Haemoptysis.
- 2-Pleural effusion.
- 3-Bronchial obstruction.

(X) BRONCHIOALVEOLAR CARCINOMA (BAC) HcQ

It is a rare peripheral tumor.

Grossly: Three patterns:

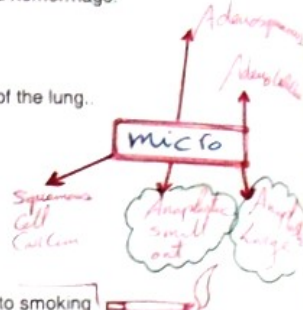
- 1)Solitary
- 2)Multicentric
- 3)Diffuse (pneumonia-like)

Microscopically:

The alveoli and bronchioles are lined by malignant cells. Two patterns:

* Predisposing Irritants
Smoke Cigarettes
Smoke air & fumes
Silicosis
Substances radioactive
SCC of lung

Central hilar main bronchus 85%
Peripheral small bronchiole 15%



Haemorrhage
infection
Distal metastases
loss of function

Solitary Multicentric Diffuse (pneumonia like)

- 1- The mucinous type : Columnar mucin secreting cells
- 2- The nonmucinous pattern: cuboidal and eosinophilic

Prognosis of BAC

- Relatively better than that of bronchogenic carcinoma
- The nonmucinous type usually occurs as a solitary tumor & has a better prognosis than the mucinous type.

* 2nd malignant neoplasms reaching

LUNG METASTASES (SECONDARIES)

ORIGIN & ROUTES OF SPREAD:

- Metastatic tumors of the lung are common & may be derived from
 - 1- Carcinomas (e.g. of thyroid, breast, kidney, placenta, GIT...etc)
 - 2- Melanoma
 - 3- Sarcomas
 - 4- Lymphoma.
- They reach the lungs through blood spread (or retrograde lymphatic spread in case of breast cancer).

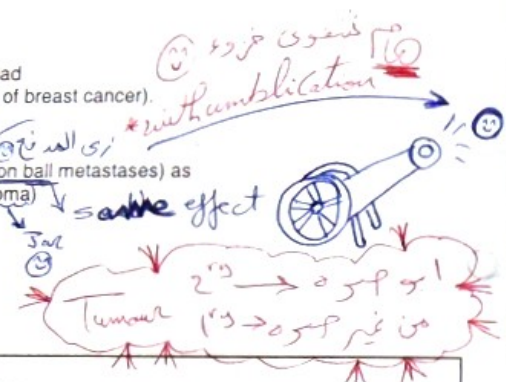
GROSS FEATURES:

- Multiple round variable-sized nodules.
- These nodules may be very large (cannon ball metastases) as in cases of renal carcinoma and seminoma.

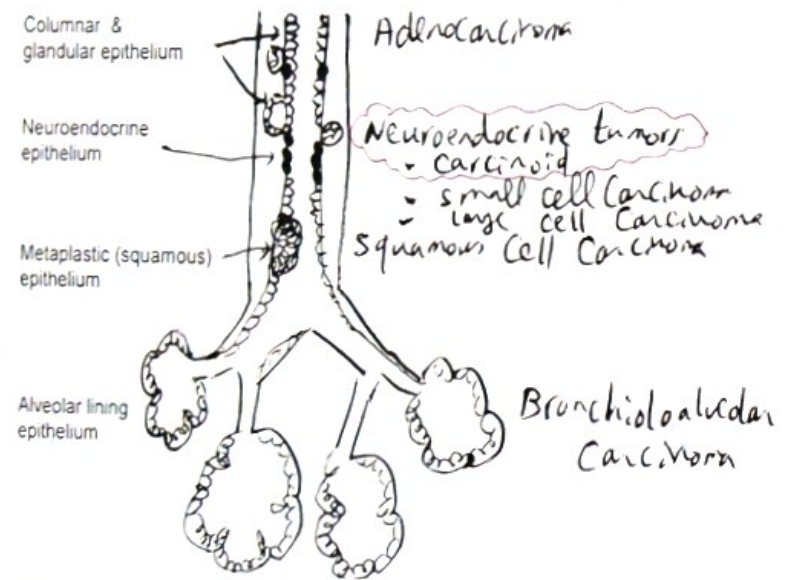
MICROSCOPY: Resembles the primary.

EFFECTS:

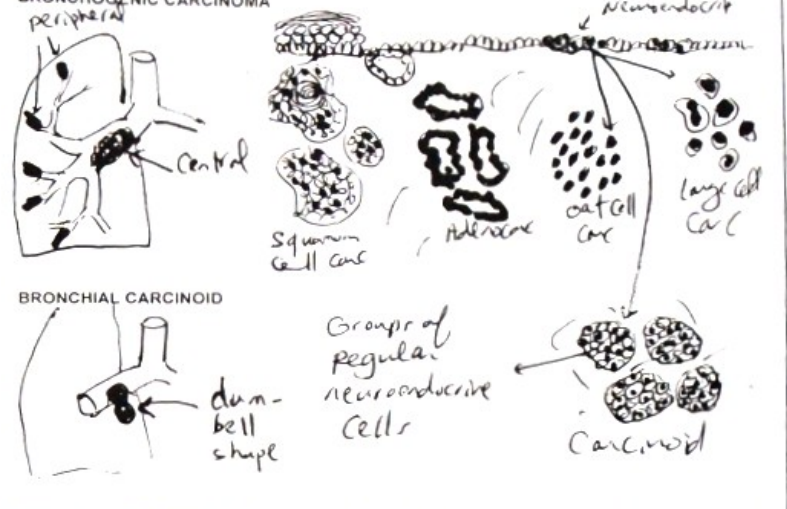
- 1) Chest pain.
- 2) Hemoptysis.
- 3) Hemorrhagic pleural effusion.



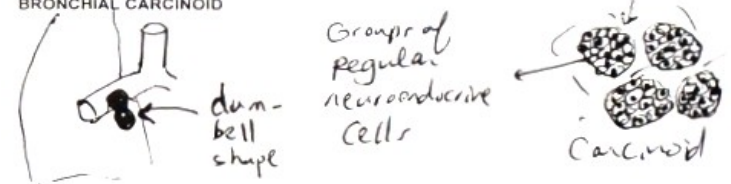
Normal Bronchial and Alveolar Lining



BRONCHOGENIC CARCINOMA



BRONCHIAL CARCINOID



as the cause of haemoptysis

(A) HAEMOPTYSIS

most common cause of chronic bronchitis

DEFINITION:

Hemoptysis is coughing blood which appears frothy (mixed with air)

CAUSES:

- 1- Diseases Of Bronchi as bronchitis, bronchiectasis, carcinoid and carcinoma.
- 2- Lung Diseases as tuberculosis, lung abscess, actinomycosis, fungal infections, chronic venous congestion, primary and metastatic tumors and traumatic injury.
- 3- General Causes Of Bleeding e.g.
 - a) hemorrhagic blood diseases (leukemia, hemophilia, purpura).
 - b) vitamin deficiency as scurvy.

Remark:

The most common causes are lung cancer, tuberculosis & chronic venous congestion.

(X) DISEASES OF THE PLEURA

SEROFIBRINOUS (FIBRINOUS) PLEURISY

AETIOLOGY:

- 1- Bacterial infections (same as in empyema...describe as above).
- 2- Viral infection.
- 3- Uraemia.
- 4- Lung infarction.
- 5- Malignant tumors of pleura (1ry or metastatic).

PATHOLOGY:

- 1-The dry type is characterized by excessive fibrin deposition on the visceral & parietal layers
- 2-The wet type is characterized by pleural effusion leading to partial or total compression collapse of the lung.
- 3-Healing may result in pleural fibrosis and adhesions.

EMPYEMA (C) *oral & MCQ*

DEFINITION:

This is suppurative inflammation of the pleura (suppurative pleurisy).

AETIOLOGY: Pyogenic bacteria (staphylococci, streptococci, pneumococci)

- 1-Direct spread from lung infections as abscess, bronchiectasis, pneumonia...
- 2-Direct spread from extra-pulmonary infections as from osteomyelitis of ribs
- 3-Penetrating chest injuries
- 4-Haematogenous spread in cases of septicaemia.

PATHOLOGY:

1-The extent of empyema may be:

- a) Diffuse (total) empyema: Pus accumulates in the whole pleural sac leading to total compression collapse of the lung.
- b) Localized empyema: Small amounts of pus localized by fibrin leading to partial collapse of the lung.

2-Pleural fibrosis and adhesions are usually extensive.

COMPLICATIONS:

- 1-Chest sinuses (empyema necessitans)
- 2-Chest deformity due to dense pleural fibrosis.
- 3-Direct spread: Pericarditis and mediastinitis.
- 4-Blood spread: Toxaemia, septicaemia and pyaemia.
- 5-Chronic empyema leading to secondary amyloidosis.

REMARK: Empyema means pus in a sac.

Pleural empyema is sometimes described as empyema thoracis, to differentiate it from other types of empyema as gall bladder empyema.

(X) HAEMOTHORAX A

Definition: Accumulation of blood in the pleural cavity

Aetiology:

- 1-Traumatic chest injuries
- 2-Malignant tumors of lung and pleura
- 3-Hemorrhagic blood diseases
- 4-Ruptured aneurysm

Effects: The accumulating blood leads to:

- 1-Compression collapse
- 2-Secondary infection may occur leading to empyema.
- 3-Healing leads to pleural fibrosis and adhesions.

(X) HYDROTHORAX

Definition:

Accumulation of serous fluid (transudate) in the pleural cavity.

Aetiology:

- Occur as apart of generalized oedema (cardiac, nutritional or renal)
- Meigs syndrome (ovarian fibroma, hydrothorax and ascites).

Effects: It leads to compression collapse

pleural cavity

PNEUMOTHORAX

air in the pleural cavity

Definition: This is accumulation of air in the pleural cavity.

Aetiology:

- 1) Traumatic chest injuries
- 2) Rupture of lung abscess or tuberculous cavity
- 3) Rupture of emphysematous bullae.

Effects:

- 1) Compression collapse of lung.
- 2) Displacement of heart, mediastinum and diaphragm.



(B) TUMORS OF THE PLEURA

1-MALIGNANT MESOTHELIOMA

DEFINITION:

A very aggressive malignant tumor arising from the mesothelial cells of the visceral or parietal pleura. Very poor prognosis.

PREDISPOSING FACTOR: Asbestosis

GROSS FEATURES:

- Early, there is a localized firm grayish white pleural mass.
- Hemorrhagic pleural effusion.
- Later, both pleural surfaces are involved & appear markedly thickened And rigid → obliteration of pleural sac
- The pleura appears thickened, rigid grayish & ensheathes the lung.

MICROSCOPY: One of three patterns:

- 1-Monophasic epithelial: It resembles papillary adenocarcinoma.
- 1-Monophasic sarcomatoid: It resembles fibrosarcoma.
- 3-Biphasic: Mixed carcinoma and sarcoma

SPREAD:

- Direct to lung, mediastinum and chest wall
- Distant (metastases):

(X) 2-BENIGN FIBROUS MESOTHELIOMA (PLEURAL FIBROMA)

- A rare tumor.
- Grossly a firm grayish localized mass with solid cut surface that may show scattered cysts.
- Microscopically: dense collagen & spindle cells with no atypia.

(X) 3-PLEURAL METASTASES

These are common tumors, most commonly derived from breast or lung carcinoma reaching the pleura by lymphatic and blood spread.

PLEURAL EFFUSION

DEFINITION:

Fluid accumulating in the pleural sac.

EXTENT: It could be mild, moderate, or massive. Some cases are unilateral, others are bilateral

TYPES:

1-Transudative (hydrothorax): see above.

2-Exudative:

a) Suppurative (empyema): see above.

b) Tuberculous: see general pathology.

c) Others as viral infection, uremia, malignant tumors (see fibrinous pleurisy)

3-Chylous (chylothorax): due to lymphatic obstruction

HEMORRHAGIC PLEURAL EFFUSION: (A) = hemothorax

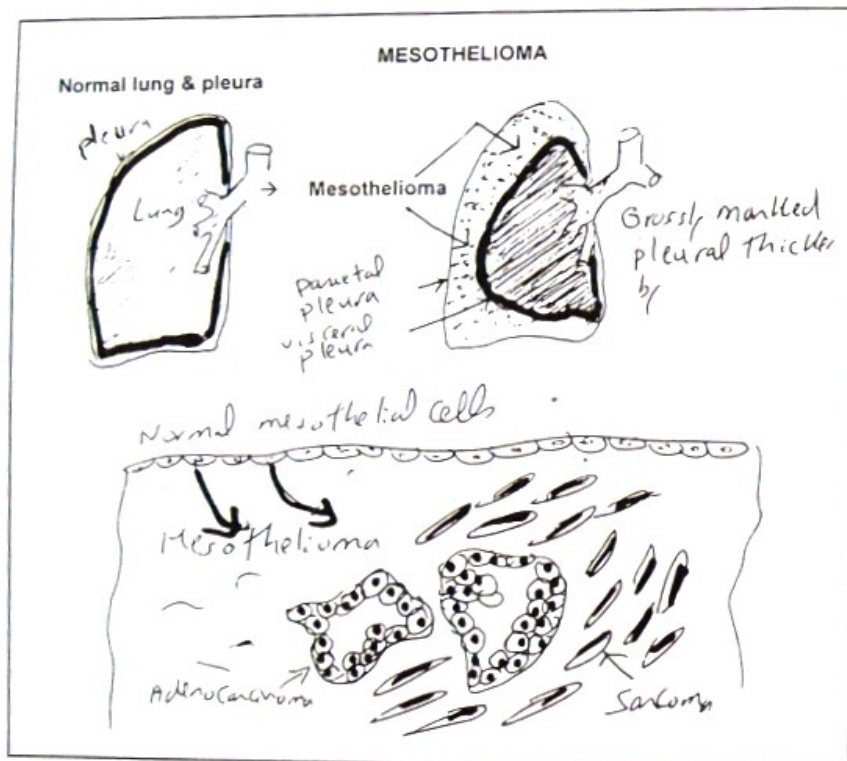
This is pleural effusion associated with hemorrhage. It is most commonly exudative. The most common causes include:

1-Primary lung carcinoma

2-Primary pleural malignancy (mesothelioma)

3-Lung and/or pleural metastases.

4-Lung/ pleural tuberculosis



THE GASTROINTESTINAL TRACT

DISEASES OF THE ORAL CAVITY

(LIPS, TONGUE, FLOOR OF MOUTH & PALATE)

INFLAMMATORY DISEASES (X)

INFLAMMATION OF LIPS (CHELEITIS)

1-**Herpes simplex**: A common viral infection of lips & oral cavity → multiple small vesicles.
2-**Others**: As suppurative inflammation, primary syphilis (chancre) & rarely Crohn's disease.

INFLAMMATION OF TONGUE (GLOSSITIS): It may be:

- 1-**Acute Glossitis**: Main types of acute glossitis include:
 - a) **Acute catarrhal (superficial) glossitis** due to hot or spicy food, smoking, superficial infections.
 - b) **Acute diffuse (parenchymatous) glossitis** due to infection of deep tongue wounds.

2-**Chronic Glossitis**: May be complicated by leukoplakia.

Types of chronic glossitis:

- a) **Nonspecific glossitis**:
 - Superficial due to chronic infection, ragged teeth or heavy smoking.
 - Nutritional due to iron or vitamin B deficiency.
- b) **Specific (granulomatous) glossitis** as tuberculosis, syphilis, fungus, sarcoidosis & Crohn's disease

Complications of chronic glossitis: → leukoplakia

Leukoplakia Of Tongue: (A) VIP + Catecholamine

Definition: Thick white mucosal patches, related to chronic irritation causing hyperplasia & keratosis.

Causes: Chronic irritation e.g. smoking, ragged tooth & diffuse syphilitic inflammation

Gross picture: Thick irregular white tongue mucosal patches.

Microscopic picture:

- 1-**Hyperplastic stratified squamous mucosa** showing **acanthosis** (increased Prickle cells) & **hyperkeratosis** (thick surface keratinized layer).
- 2-**The underlying submucosa** shows chronic inflammation.

Effects: Leukoplakia is precancerous that may → squamous cell carcinoma

3-Other Types of Glossitis as:

- a) **Aphthous glossitis** and **stomatitis** (see aphthous ulcers of the tongue).
- b) **Geographic tongue** (benign migratory glossitis): a relatively common condition of unknown cause characterized by an inflamed erythematous flat zone at tongue dorsum (with loss of papillae)

INFLAMMATION OF ORAL MUCOSA (STOMATITIS):

- 1-**Catarrhal stomatitis** due to hot or spicy food, smoking or infections.
- 2-**Herpes simplex virus infection** (herpetic stomatitis).
- 3-**Moniliasis** (see general pathology) = *Candida* (HcQ)
- 4-**Aphthous stomatitis & glossitis** (see tongue ulcers)
- 5-**Vincent's angina**: **necrotizing inflammation** caused by organisms as *Treponema vincenti* (HcQ)
- 6-**Agranulocytic angina**: Inflammation and necrosis seen in cases of agranulocytosis.
- 7-**Granulomas** as T.B, sarcoidosis, Crohn's disease, histoplasmosis, Wegener's granulomatosis.

cheilitis
glossitis
stomatitis
acute
chronic

*predisposing factors of GIT = 5(S)
1 Spicy food
2 Smoke & cigarettes
3 Spirits & alcohol
4 Sex (syphilis)
5 in oral cavity sharp tooth

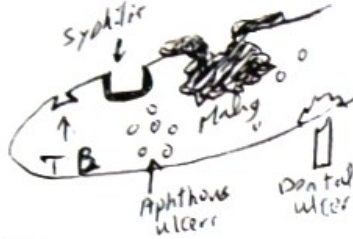
White tongue disease

ULCERS OF THE ORAL CAVITY

These most commonly affect the tongue.

ULCERS OF THE TONGUE INCLUDE:

- ★ **1-Dental Ulcer:** Shallow traumatic ulcer occurs at the edge of the tongue near a sharp tooth.
- ★ **2-Aphthous Ulcers**
 - Extremely common.
 - They are multiple, small superficial painful ulcers (less than 5 mm in diameter).
 - More common in children & young adults.
 - Unknown aetiology (? autoimmune).
 - They usually resolve in few weeks, but may recur.
 - They were formerly called **dyspeptic ulcers**.
- ★ **3-Tuberculous Ulcer:**
 - An ulcer with undermined edges and caseous floor.
 - It most commonly develops at the tip of tongue in cases of Cavitary pulmonary tuberculosis. Coughed sputum containing tubercle bacilli → o infection of the tongue.
- ★ **4-Syphilitic Ulcers:**
 - Primary stage of syphilis: ulcerated chancre.
 - Secondary stage: ulcerated mucous patches.
 - Tertiary stage: gummatous ulcer, precancerous.
- ★ **5-Malignant Ulcer:**
 - Most common in anterior two thirds of tongue.
 - Less common in the posterior 1/3.
 - The edges are raised everted, the floor is rough and necrotic and the base is indurated.



(A) TUMORS OF THE ORAL CAVITY

Benign & malignant tumors of lips, tongue and mouth are almost similar and include:

A) BENIGN TUMORS:

- 1-Squamous cell papilloma (see general pathology)
- 2-Capillary hemangioma
- 3-Pyogenic granuloma ★★ MCQ
It is a capillary hemangioma associated with septic inflammation. It is sometimes considered as a richly vascularized granulation tissue in response to localized infection.
- 3-Cavernous hemangioma & lymphangioma (hamartomas):
May cause macrochelia or macroglossia.
- 4-Adenomas of minor salivary glands
- 5-Fibroma, leiomyoma & schwannoma.
- 6-Granular cell tumor: A rare benign tumor, mainly occurs in tongue. It consists of large cells with granular cytoplasm & is believed to be of neurilemmal origin.

B) MALIGNANT TUMORS

- 1-Carcinomas:
 - squamous cell carcinoma (most common)
 - malignant mixed tumor of minor salivary glands..
 - Basal cell carcinoma may occur in lips.
- 2-Sarcomas as angiosarcoma, Kaposi's sarcoma, fibrosarcoma.
- 3-Malignant melanoma & lymphomas.

SQUAMOUS CELL CARCINOMA OF THE TONGUE (A) + Jaz + Case

Predisposing factors:

- Leukoplakia ★
- Tobacco use.
- ★ Human papilloma virus infection (types 11, 16, 18).
- Tertiary syphilis.

Sites: The anterior 2/3 of tongue is more common than the posterior 1/3.

Gross:

- 1-Exophytic patterns:
 - Fungating polypoid pattern.
 - Verrucal pattern: A fungating papillary growth.
- 2-Endophytic patterns:
 - Ulcerative pattern is the most common: The malignant ulcer is irregular with everted edges, necrotic floor and indurated base).
 - Diffuse infiltrating pattern: Uncommon

Microscopy:

- 1-Squamous cell carcinoma may be
 - Well differentiated
 - Moderately differentiated (commonest)
 - Poorly differentiated.
- 2-Verrucal carcinoma:
 - It is a form squamous carcinoma formed of papillary groups of very well differentiated squamous cells showing minimal atypia
 - It has a limited tendency of invasion

Spread:

- 1-Direct: This may lead to fixation of the tongue to the floor of the mouth.
 - 2-Lymphatic spread to the regional (cervical) lymph nodes
Lymphatic spread is common due to rich lymphatics of the tongue & due to tongue movements.
 - 3-Blood spread (distant metastases) occurs late. LBLB
- Prognosis:** → disordered + discharge of ear
- 1-Verrucous carcinoma has the best prognosis
 - 2-Carcinoma of anterior 2/3 of tongue is better than of the posterior 1/3

SQUAMOUS CELL CARCINOMA OF THE LIP:

Predisposing factors: Leukoplakia, smoking & papilloma virus infection.

Site: It is more common in the lower lip.

Grossly:

- 1-Exophytic fungating polypoid or verrucal patterns.
- 2-Endophytic ulcerative pattern (most common) or infiltrative patterns

Microscopically: Squamous cell carcinoma (usually moderately or well differentiated)

Spread:

- 1-local → mandible
- 2-lymphatic → cervical lymph nodes
- 3-Blood (late)
- 4-Rarely carcinoma of one lip leads to malignant implantation on the other lip.

SQUAMOUS CELL CARCINOMA OF THE MOUTH:

It affects floor of mouth, lining of cheeks, gums and/or palate.

Grossly: it may be exophytic or endophytic

Microscopically:

Squamous cell carcinoma (usually moderately or well differentiated).

Spread:

- 1)local
- 2)lymphatic to cervical lymph nodes
- 3)blood spread is late.

mostly lower lip
syphilis in upper lip
Mechanism of invasion

DISEASES OF THE SALIVARY GLANDS

(X) INFLAMMATIONS (SIALADENITIS)

Commonest in parotid gland (parotitis)

1-Mumps: (Acute viral parotitis, epidemic parotitis):

- **Children:** Rare in adults
- **Aetiology:** Mumps virus, transmitted by droplet infections.
- **Incubation period:** 2-4 weeks
- **Gross:** Bilateral parotid enlargement
- **Microscopy:**
 - a) Acini show cytoplasmic inclusion bodies & cell degeneration
 - b) Interstitial inflammation: lymphocytes, plasma cells & macrophages
- **Complications:**
 - a) Viral sialadenitis of other salivary glands
 - b) Orchitis: particularly in adults. This may lead to infertility.
 - c) Oophoritis
 - d) Others: Pancreatitis, thyroiditis, mastitis, meningoencephalitis.



2-Cytomegalic inclusion disease: see general pathology.

3-Acute suppurative parotitis (parotid abscess):

- **Aetiology:** predisposed to by diabetes & poor oral hygiene. caused by staphylococcal infection.
- **Pathology:** Swollen gland containing pus.
- **Complications:** spread → lymphadenitis, toxemia, pyemia...etc

4-Chronic obstructive (calcular) sialadenitis:

Caused by obstruction of salivary ducts by stones.

5-Benign lymphoepithelial lesion (Mikulicz disease):

A rare autoimmune disease characterized by diffuse lymphocytic infiltrate and atrophy of gland epithelium.

TUMORS OF SALIVARY GLANDS (A)

Benign:

- 1-Pleomorphic adenoma (commonest).
- 2-Monomorphic adenomas as:
 - Papillary cystadenoma lymphomatosum,
 - Tubular (canalicular) adenoma
 - Basal cell adenoma
 - Others as oxyphil adenoma/ oncocytoma, sebaceous adenoma.

Malignant:

- 1-Malignant mixed salivary tumor is the commonest.
- 2-Adenoid cystic carcinoma.
- 3-Mucoepidermoid carcinoma.
- 4-Acinar cell carcinoma.
- 5-Others as myoepithelial carcinoma, basal cell adenocarcinoma, oncocytic carcinoma, clear cell carcinoma...

PLEOMORPHIC ADENOMA (Benign mixed salivary tumor)

It is the commonest salivary tumor.

Parotid is the most common site.

More common in females.

Gross: A capsulated, lobulated firm mass mostly arises at lower pole of parotid, 2-5 cm in diameter. Cut section shows mucinous foci, cystic foci and solid foci.

Microscopy:

- Proliferating epithelial cells forming acini and cords.
- Proliferating myoepithelial cells.
- Fibrous stroma with myxomatous & cartilaginous islands (pseudocartilage).

Behavior:

- Tiny prolongations of tumor tissue commonly perforate the capsule.
- Therefore recurrence is common after surgical excision.
- True malignant transformation may occur and is evidenced by:
 - Rapid increase in size, with induration and fixation
 - Facial nerve paralysis (due to invasion)
 - Regional lymph node enlargement (due to spread)

PAPILLARY CYSTADENOMA LYMPHOMATOSUM (Warthin's tumor)

The former tumor name adenolymphoma is no more used. Tumor is more common in parotid. More common in males.

Gross: Capsulated cystic mass with papillae.

Microscopy:

- It is papillary cystadenoma with cystic spaces lined by uniform double-layered oncocytic (eosinophilic) epithelium.
- The stroma is rich in lymphocytes.

* MALIGNANT MIXED SALIVARY TUMOR:

Origin: De novo or on top of pleomorphic adenoma.

Gross: Noncapsulated irregular infiltrative growth with areas of hemorrhage & necrosis.

Microscopy:

- Carcinomatous elements which may be adenocarcinoma, squamous cell carcinoma or anaplastic carcinoma.
- Pleomorphic stroma with myxomatous & pseudocartilagenous foci.

Spread:

- **Local:** to facial nerve and surrounding structures.
- **Distant spread:** mainly by lymphatics to cervical lymph nodes. Blood: late to lungs, bones, liver, brain.

* ADENOID CYSTIC CARCINOMA (Cylindroma):

It affects minor or major salivary glands & arises from ducts.

Grossly, it appears as yellowish infiltrative growth.

Microscopically, it consists of groups of small sized malignant cells, commonly arranged around small patent ductular spaces in a cribriform manner. Perineural invasion is a very common microscopic finding.

Spread:

- **Local spread:** The tumor is a commonly slowly growing (indolent). Perineural invasion is very frequent
- **Distant spread:** ultimately occurs; mainly by blood to lungs & bone, rarely by lymphatics).

* MUCOEPIDERMOID CARCINOMA:

It is a rare malignant tumor arising from ducts.

Grossly it forms an infiltrative growth that may show mucin-filled cysts.

Microscopically it consists of a mixture of malignant squamous cells, mucin secreting cells & intermediate cells. The tumor may be well, moderately or poorly differentiated.

Spread:

- **Direct spread:** The may grow slowly (indolent) or rapidly depending on degree of tumor differentiation
- **Distant spread** mainly by lymphatics. High grade tumors also spread by blood (to lungs & bone)

2011 Classify salivary tumours and discuss one of Malignant

Handwritten notes in a cloud shape: "Malignant transformation due to invasion of facial nerve & lymph nodes" with arrows pointing to the facial nerve and lymph nodes in the diagram above.

Handwritten notes in a cloud shape: "Aetiology: no radiation don't waste SSSSS"

Handwritten notes in a cloud shape: "Partial + Prostate + Pancreas + Stomach + Rectum + Malignant Tumors"

Handwritten notes in a cloud shape: "Complications: Haemorrhage, infection, Distant metastasis"

Vertical handwritten note: "Malignant lymphoma"

(X) ACINIC CELL CARCINOMA:

A rare tumor affecting major or minor salivary glands & arises from acini

Grossly: it is usually small and fairly defined firm grayish mass.

Microscopically it consists of large cells with clear or finely granular cytoplasm, arranged in sheets or acini.

Spread:

It grows slowly (indolent) with frequent local recurrence after excision

Can rarely metastasize.

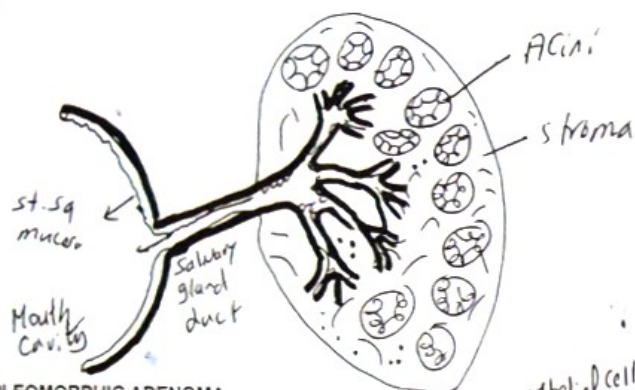
MCQ

REMARK: Causes Of Parotid Enlargement

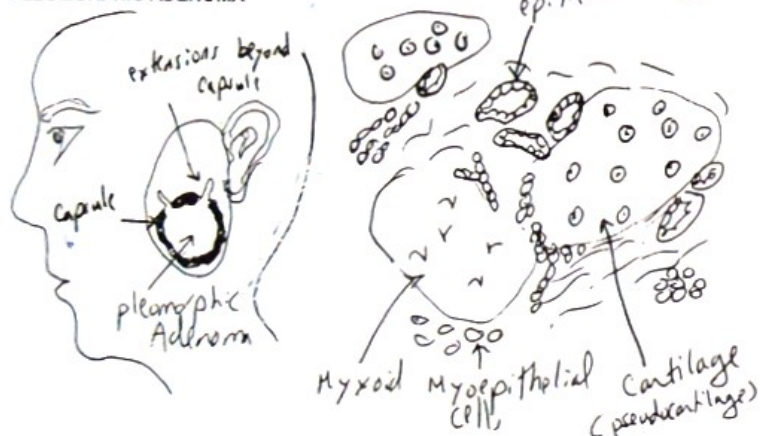
- 1) Parotitis (enumerate)
- 2) Tumors (enumerate)

MCQ = very rare Metastasize

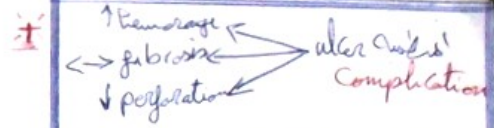
NORMAL SALIVARY GLAND



PLEOMORPHIC ADENOMA



What is GERD!!!



DISEASES OF THE OESOPHAGUS

ULCERS OF THE OESOPHAGUS

TYPES AND CAUSES:

- 1- Malignant ulcer (ulcerative carcinoma): everted edges, indurated base...
- 2- Peptic ulcer may occur at the lower third of oesophagus in association with reflux oesophagitis.
- 3- Traumatic ulcer following instrumentation.
- 4- Corrosive ulcers due to accidental or suicidal swallowing of caustic chemicals as potassium hydroxide
- 5- Tuberculous ulcer due to swallowing of infected sputum in patients with lung T.B.

EFFECTS:

- 1- Hematemesis
- 2- Fibrous stricture.

(B) OESOPHAGITIS

A) REFLUX OESOPHAGITIS

(Gastro esophageal Reflux Disease GERD):

Aetiology:

Repeated reflux of the gastric contents → prolonged exposure of the oesophageal mucosa to the acidic contents of the stomach. Reflux may be due to:

- 1- Incompetence of lower oesophageal sphincter or (Partial incompetence)
- 2- Hiatus hernia (protrusion of part of the stomach through the diaphragmatic hiatus).

Gross: Redness and superficial erosions of the lower oesophageal mucosa.

Microscopy:

Mucosal epithelial hyperplasia
Intraepithelial neutrophils and eosinophils.

Barrett's metaplasia (see below) which may be followed by dysplasia

Complications:

- 1- Barrett's oesophagus: This is intestinal glandular metaplasia occurring within the squamous oesophageal mucosa. It may be followed by metaplasia. It is precancerous → adenocarcinoma
- 2- Peptic ulceration and fibrous stricture.

B) OTHERS as:

Monilial (fungal), viral, radiation & uremic oesophagitis..

OESOPHAGEAL DIVERTICULA (X)

Definition: These are saccular outpouchings of the oesophageal wall.

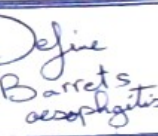
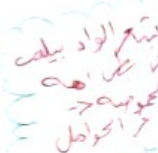
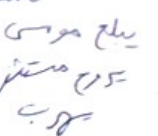
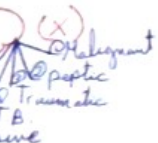
Aetiology:

Congenital or acquired weakness of the musculosa of oesophagus
Increased intraluminal pressure (as in cases of achalasia).

Sites: The most common sites of diverticula are:

- 1- Posterior aspect of the pharyngo-oesophageal junction (Pulsion diverticulum).

- This occurs in patients with their cricopharyngeus muscles failing to relax during deglutition → rise of intrapharyngeal pressure → mucosal pouching from in between the weak muscle fibers at the posterior aspect.
- The diverticulum accumulates food → compression of oesophagus → dysphagia.



2- Above achalasia of the lower oesophageal sphincter.

3-Traction diverticulum:

- It occurs at the anterior aspect of the midportion of oesophagus opposite the tracheal bifurcation due to fibrous adhesive traction ; e.g. from fibrotic tuberculous lymph nodes

TUMORS OF THE OESOPHAGUS

BENIGN:

- 1) Squamous cell papilloma
- 2) Leiomyoma
- 3) Others as fibroma, lipoma, schwannoma ...etc

MALIGNANT:

- 1) Carcinoma
- 2) Sarcomas as leiomyosarcoma & fibrosarcoma
- 3) Malignant gastrointestinal stromal tumor (malignant GIST)
- 3) Others as lymphoma

CARCINOMA OF THE OESOPHAGUS:

Predisposing Factors:

- Age: usually above the age of 40.
- Sex: More common in males except for the rare post-cricoid carcinoma which predominates in females.
- Diet: a) Habitual ingestion of hot foods and drinks b) Vitamin deficiency (A, B & C).
- Smoking: and heavy alcohol intake.
- Achalasia of the lower oesophageal sphincter.
- Plummer-Vinson syndrome: see below.
- Barrett's oesophagus.

Sites:

Commonest in middle 1/3, then lower 1/3. Rarest is upper 1/3.

Gross picture:

- 1- Polypoid fungating pattern.
- 2- Malignant ulcer (raised everted edges, rough floor & indurated base).
- 3- Infiltrative pattern leading to annular stricture.

Microscopy:

- 1- 95% of cases: Squamous cell carcinoma.
- 2- 5% of cases: Adenocarcinoma (when it arises in the lowest part).

Spread:

- 1- Direct to trachea and mediastinal structures.
- 2- Lymphatic → supraclavicular, celiac and mediastinal lymph nodes.
- 3- Blood (late) to lungs, liver....

Clinical effects:

- 1- Oesophageal obstruction.
- 2- Hematemesis
- 3- Tracheo-oesophageal fistula.

(X) OESOPHAGEAL OBSTRUCTION

1-ORGANIC CAUSES:

- Lumen obstruction by tumor, foreign body or large bolus of food
- Wall stricture:
 - a) congenital
 - b) Acquired: e.g. post inflammatory (particularly corrosive) & stricture carcinoma
- Outside compression by mediastinal tumors, enlarged lymph nodes, retrosternal goiter, oesophageal diverticulum.

2-FUNCTIONAL CAUSES:

- Achalasia of lower oesophageal sphincter (achalasia of the cardia): Achalasia means inadequate relaxation of a sphincter. Aetiology is unknown. May be due to idiopathic degenerative changes affecting the vagal branches supplying the oesophagus. Achalasia leads → dysphagia with hypertrophy and dilatation of oesophagus above the lower oesophageal sphincter. In 2-7% of prolonged cases, oesophageal carcinoma develops.
- Plummer-Vinson syndrome: It affects middle aged females and is characterized by dysphagia, iron deficiency anemia and sometimes post cricoid carcinoma

HEMATEMESIS (A) VIP

DEFINITION: Vomiting of blood (usually brownish and mixed with food material). If this blood passes with stool it will appear dark brown (melena). Therefore causes of hematemesis & melena are the same.

CAUSES:

1-OESOPHAGEAL CAUSES:

- a) Oesophageal Varices: + peptic ulcer
Definition: This is varicosity of the oesophageal veins at the submucosa of the lower part of oesophagus. The veins appear dilated, tortuous and engorged with blood.
Aetiology: It is due to portal hypertension seen in cases of:
 - Cirrhosis
 - Bilharzial hepatic fibrosis
 - Portal vein obstruction due to thrombosis or malignant invasion.
- b) Oesophageal Carcinoma
- c) Oesophagitis & oesophageal ulcers (enumerate)
- d) Aortic aneurysm rupturing into the oesophagus.
- e) Malignant mediastinal tumors infiltrating the oesophagus

2-GASTRIC CAUSES:

- a) Gastritis b) Peptic ulcers c) Acute ulcers d) Tumors.

3-DUODENAL CAUSES:

- a) Duodenitis b) Peptic ulcers c) Acute ulcers d) Tumors

4-GENERAL CAUSES OF BLEEDING:

- a) Blood diseases (as leukemia, purpura)
- b) Vitamin C or K deficiency.

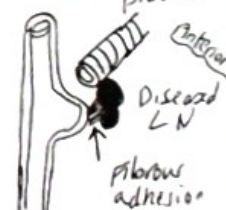
c) Traumatic causes → Cough

OESOPHAGEAL DIVERTICULA

Posterior



PULSION DIVERTICULUM



TRACTION DIVERTICULUM

What is commonest cause of hematemesis in oesophageal cases? (peptic ulcer)

* Congenital diseases → lig → stomach
 * Kidney

DISEASES OF THE STOMACH

(X) GASTRIC OBSTRUCTION

Occurs at pyloric region due to:

1- Congenital pyloric stenosis:

- A disease of newly born infants.
- It is due to congenital defects of the autonomic supply to pyloric sphincter.
- The pyloric sphincter is rigid & thickened.
- Effects: Regurgitation & vomiting leading to dehydration and alkalosis.

2- Acquired causes: Tumors and healed peptic ulcer.

GASTRITIS (A) V.I.P.U.R

ACUTE GASTRITIS

Aetiology:

- 1- Drugs as nonsteroidal anti-inflammatory drugs & cytotoxic drugs
- 2- Excessive alcohol consumption
- 3- Excessive cigarette smoking
- 4- Uremia → renal failure
- 5- Irritant or spicy food
- 6- Systemic infection: as salmonellosis
- 7- Severe stress, ischemia and shock
- 8- Chemical irritation by strong alkalis or acids (as in suicidal attempts).
- 9- Mechanical trauma as during endoscopic examination
- 10- Gastric irradiation

Pathology:

- 1- Catarrhal inflammation (describe) → hyperemic swollen oedematous mucous (gross)
- 2- Erosive (ulcer) & hemorrhagic gastritis

CHRONIC GASTRITIS

AETIOLOGY:

- 1- Infective: Chronic bacterial infection with *Helicobacter pylori*
- 2- Chemicals & toxins: e.g.:
 - Bile reflux (e.g. post-operative after gastrojejunostomy)
 - Drugs
 - Alcoholism, smoking, chronic uremia
- 3- Immunologic (autoimmune), may be associated with pernicious anaemia.
- 5- Granulomatous as Crohn's disease
- 6- Others: as radiation and amyloidosis.

PATHOGENESIS:

It varies according to the aetiological factor:

1- In Chronic *Helicobacter pylori* infection:

- Bacteria exist in the surface mucosa & are best stained by Giemsa's stain
- The bacteria secrete urease enzyme → ammonia production → Protection of these bacteria from gastric HCL
 - Toxic effect on gastric mucosa → gastric peptic ulcer.
 - The bacteria also produce protease → breaks gastric mucus → loss of the protective mucus layer → gastric peptic ulcer.
 - These bacterial enzymatic activities lead to a state of continuous destruction and retarded healing → atrophic gastritis.
 - Moreover, gastric hyperacidity is common → duodenal peptic ulcer
- Mechanism is not clear but is believed to be due to effect of *H. pylori* products on parietal cells which makes the cells less responsive to gastrin → feedback → moderate hypergastrinemia → HCl secretion

gastric carcinoma
 autoimmune gastritis
 macrocytic anemia

no intrinsic factor
 macrocytic anemia
 no iron

2- In autoimmune gastritis: There are autoantibodies against the gastric parietal cells and intrinsic factors, which are located mainly in the corpus.
 → atrophy of acid and intrinsic factor secreting cells → hypoacidity & anaemia.

PATHOLOGICAL FEATURES & HISTOLOGICAL TYPES:

1- Chronic superficial gastritis:

- This is the early stage
- The lamina propria shows lymphocytes & plasma cells
- Neutrophils may appear denoting high inflammatory activity.
- No mucosal gland atrophy.

2- Chronic atrophic gastritis:

- This is an advanced stage
- There is marked loss of glandular structures, associated with fibrosis, together with lymphocytes & plasma cells
- It is graded as mild, moderate and severe.
- In severe cases, atrophy is seen without inflammatory cells (gastric atrophy).
- Intestinal metaplasia may occur.
- Dysplasia may develop and may progress to carcinoma in situ or invasive carcinoma (particularly with *H. pylori* gastritis).

ANOTHER CLASSIFICATION

1- Type A gastritis (autoimmune gastritis) that affects fundus and body and is associated with hypochlorhydria and pernicious anaemia

2- Type B gastritis (nonimmune gastritis) which is further subdivided into:

- a- Hypersecretory antral gastritis characterized by hyperchlorhydria → duodenal peptic ulcer.
- b- Environmental gastritis (type AB gastritis) characterized by affection of antrum and fundus, commonly associated with the development of gastric peptic ulcer.

non inflammatory HYPERTROPHIC GASTROPATHY (X)

- A group of uncommon non inflammatory gastric lesions characterized by mucosal rugal enlargement with mucosal hyperplasia. May be associated with hyperacidity & multiple peptic ulcers
- The most common type is Menetrier's disease.

ULCERS OF THE STOMACH AND DUODENUM

These include: a) Acute ulcers b) Chronic peptic ulcers c) Malignant ulcer.

ACUTE ULCERS OF STOMACH & DUODENUM (A)

- Acute ulcers are multiple superficial and hemorrhagic.
- They are seen in cases of acute gastritis due to drugs, infection, severe stress e.g. severe burns (stress ulcers) as well as in cerebrovascular accidents and all cases of acute increase of gastric acidity.
- They heal with minimal fibrosis.

CHRONIC PEPTIC ULCERS (A) V.I.P

DEFINITION: Peptic ulcer is simply a defect within the mucosa of any portion of the gastrointestinal tract exposed to acid-pepsin secretion.

SITES:

- 1- Duodenum: first portion (80% of peptic ulcers occur in the duodenum).
- 2- Stomach: usually antral (18% of peptic ulcers occur in the stomach).
- 3- Within a Barrett's oesophagus.
- 4- In the margins of gastrojejunostomy. This ulcer is called stomal ulcer.
- 5- Within a Meckel's diverticulum containing ectopic gastric mucosa.

Complication:

1. fibrosis → stricture
2. No spread of inflammation
3. pit. can. Colours

C. Superficial G.	C. atrophic G.
• no mucosal gland atrophy	• Marked loss of glands → atrophy
• Inflammatory activity neutrophils	• no inflammatory cells
• no Dysplasia	• Dysplasia
• no Carcinoma in situ	• Carcinoma in situ

White Knight

SEX: Male to female ratio is 3 : 1.

AGE: Usually above the age of 20 years

AETIOLOGY:

Predisposing factors:

- Habitual smoking, intake of spicy food
- Nonsteroidal anti-inflammatory drugs
- High or repeated doses of corticosteroids
- Mental stress.

Pathogenesis:

1-Duodenal ulcers are caused by:

a) **Hyperacidity:** This may occur in cases of:

H. pylori gastritis causing excess HCL secretion. This is the most common cause

Zollinger Ellison syndrome: Pancreatic gastrin secreting tumor called gastrinoma → hyperacidity → multiple peptic ulcers

Chronic stress with high vagal tone

b) **Genetic (hereditary) predisposition:**

The genetic defect is decrease of the normal defense mechanisms (surface mucus & mucosal prostaglandins). Evidence of genetic Predisposition includes:

- Duodenal ulcers have a **familial tendency**
- Duodenal ulcers are most commonly observed in **blood group O persons** (30 times more liable to develop duodenal ulcer than other blood groups).

2-Gastric ulcers

Not caused by hyperacidity (gastric HCl in cases of gastric ulcer may be normal or even lower than normal).

No genetic predisposition

The possible causes of gastric ulcers include:

a) **Mucosal devitalization** by one or more of the following factors:

- H. pylori gastritis** (by enzymatic effects and not by hyperacidity).
- Localized mucosal ischemia (microthrombi).
- Duodenal-gastric reflux → chemical mucosal injury by bile & pancreatic juice.
- Delayed gastric emptying.
- Impaired mucus-bicarbonate barrier

b) **Traumatic effect of food** is a helping factor.

Role of H. pylori infection in peptic ulcers of duodenum & stomach:

H. pylori infection of gastric mucosa is present in > 90 of cases of duodenal peptic ulcer and in about 70% of cases of gastric peptic ulcer. The ulcerogenic effect of H. pylori on gastric & duodenal mucosa has been described before (see chronic gastritis)

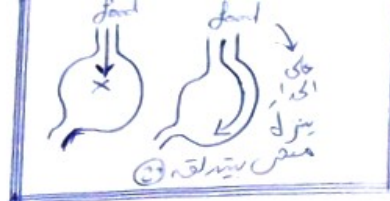
PATHOLOGY:

Gross Features:

	DUODENAL ULCER	GASTRIC ULCER
★ Location:	First part, anterior or posterior.	Pyloric antrum at lesser curvature.
★ Size:	1-3 cm.	1-3 cm
★ Shape:	Round or oval	Round, oval or saddle shaped.
★ Edges:	Sharp or sloping	Sharp or sloping
★ Floor:	Smooth	Smooth
★ Base:	Indurated due to fibrosis.	Indurated due to fibrosis

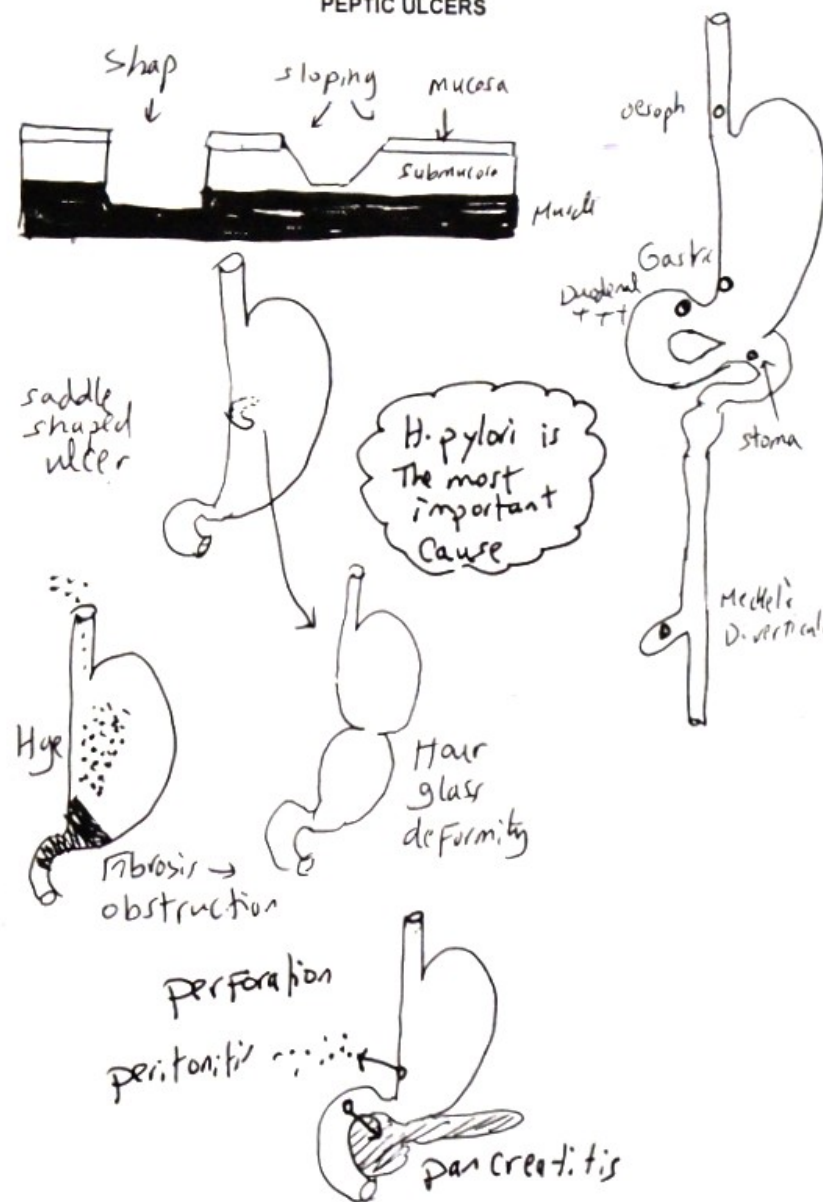
Microscopic Features:

- The top (superficial) part of the ulcer shows necrotic debris.
- The deeper part shows chronic inflammatory cells and fibrosis.



التهاب المعدة المزمن
مترادف
التهاب المعدة المزمن

PEPTIC ULCERS



gastrea ulcer
بطن كسرطان
و بطن كسرطان
gastrea ulcer



COMPLICATIONS:

- 1- Hemorrhage: It leads to hematemesis and melena.
- 2- Perforation (10% of cases).
- Peritonitis occurs (mainly in case of gastric ulcer).
- Perforated duodenal ulcer may → pancreatitis.
- 3- Fibrosis and fibrous contraction may lead to:
- Duodenal stenosis
- Pyloric stenosis.
- Hour glass deformity of stomach due to fibrosis of a saddle ulcer.
- 4- Malignant change: It occurs in <1% of gastric ulcers.
- Duodenal ulcers are not precancerous.

TUMORS OF THE STOMACH

A) BENIGN TUMORS:

- 1- Adenomatous Polyp (adenoma):
- Gross: Usually single. Sessile, pedunculated or branching.
- Microscopy: Proliferated mucosal glands showing dysplasia.
- Effects:
1) Hematemesis or melena (due to ulceration)
2) Pyloric obstruction
3) It is precancerous.
- 2- Gastrointestinal stromal tumor (GIST): benign
- 3- Others as leiomyoma schwannoma, neurofibroma, fibroma, lipoma & angioma

B) MALIGNANT TUMORS

- 1- Carcinoma
- 2- Carcinoid
- 3- Lymphoma
- 4- Sarcomas as leiomyosarcoma, fibrosarcoma & liposarcoma.
- 5- Gastrointestinal stromal tumor (GIST): malignant

Remark: GIST: ★ benign & malignant

- These tumors are not uncommon.
- They arise in any part of GIT, most commonly the stomach.
- They consist of proliferated spindle cells that express a tumor marker called CD117 (c-kit).
- Their behavior is unpredictable; may be benign or malignant

(A) CARCINOMA OF THE STOMACH

SEX & AGE: More common in males above the age of 40 years.

PREDISPOSING FACTORS:

- 1- Chronic gastritis.
- 2- Adenomatous polyp.
- 3- Peptic ulcer.
- 4- Blood group A persons.
- 5- Smoked food or foods containing nitrites.

SITES: Anywhere in stomach, but most common in pyloric antrum & in cardia. → Same 5 before

GROSS:

- 1- Fungating polypoid type: A large projecting polypoid mass.
- 2- Ulcerative type: A large irregular ulcer with everted edges, necrotic floor and indurated base.
- 3- Infiltrative type: One of 2 patterns; both invade musculosa or deeper:
- Localized infiltrative pattern affecting the pyloric region which appears thickened & rigid, associated with dilatation of the rest of the stomach due to pyloric stenosis.

رأس بوشين ← اكل اكلide ولم يتصوره لا اكله من الكبد
عالم مشهور روسي هو دي

- Diffuse infiltrative growth: The whole stomach appears rigid and small (leather bottle stomach or linitis plastica).
- Superficial spreading type: Characterized by infiltration limited to mucosa and submucosa which appear indurated. Musculosa is free.

MICROSCOPY:

- Microscopic types:
1- Adenocarcinoma (see general pathology & describe).
2- Mucoid carcinoma
3- Signet ring cell carcinoma (describe)
4- Undifferentiated (anaplastic) carcinoma. & squamous cell carcinoma
- Microscopic extent of invasion include
1- Early gastric carcinoma (superficial spreading type) in which malignancy is confined to mucosa and submucosa with no deep invasion.
2- Advanced gastric carcinoma (deeply invasive).

SPREAD:

- 1- Direct → pancreas, colon, liver, spleen.
- 2- Lymphatic → gastric, celiac, paraortic and left supraclavicular lymph nodes.
- 3- Blood spread (portal) → liver then lungs, bones...etc.
- 4- Transcoelomic spread.
→ Peritoneal metastases and hemorrhagic ascites.
→ Krukenberg tumors (bilateral ovarian metastases).

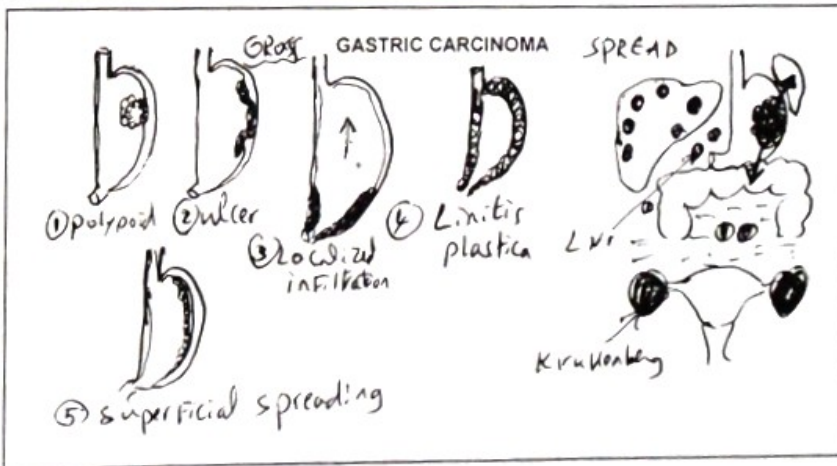
OTHER EFFECTS: = complication

- 1- Hematemesis and melena (dark altered blood passing with stools).
- 2- Pyloric obstruction.
- 3- Mucosal destruction leading to hypochlorhydria and intrinsic factor deficiency.
- 4- Anaemia due to loss of blood and deficiency of intrinsic factor.

LYMPHOMA OF THE STOMACH

It is next in frequency to gastric carcinoma. The most common types include:

- 1- MALT lymphoma (mucosa associated tissue lymphoma: This is a low grade indolent small B cell lymphoma)
- 2- Large B cell lymphoma: This is a high grade lymphoma



DISEASES OF THE INTESTINE

INFLAMMATIONS

(X) TYPHOID FEVER

Definition: A systemic infective disease caused by *Salmonella typhi*. It affects intestine & other organs.

Aetiology and Pathogenesis:

- Ingestion of food or drink contaminated with *Salmonella typhi*.
- During the **incubation period** (2 weeks) no intestinal lesions are produced, but the following occur:
 - 1-Macrophages carry the typhoid bacilli to the Peyer's patches where these bacilli proliferate.
 - 2-Bacilli invade lymphatics then blood (typhoid bacteraemia)
 - 3-Bacilli are removed from blood by reticuloendothelial cells.
 - 4-Bacilli proliferate inside the reticuloendothelial cells.
 - 5-At the end of incubation period these reticuloendothelial cells die and large number of typhoid bacilli reach the blood (typhoid septicaemia).
- The disease** is manifested after the incubation period & lasts for 5 weeks. It consists of:
 - 1-Toxaemia (headache, fever, anorexia...etc) due to bacterial endotoxins.
 - 2-Invasion of intestine (main site) and other organs producing typhoid lesions.
- The tissue reaction** within these lesions consists of macrophages (with no or few neutrophils).

Pathology:

Intestinal lesions:

- Peyer's patches of small intestine and solitary follicles of large intestine show:
- 1-During 1st week of illness: They become swollen due to hyperemia & typhoid reaction
 - 2-During the 2nd week: Necrosis of the overlying mucosa.
 - 3-During the 3rd week: The necrotic mucosa separates. Typhoid ulcers occur & appear:
 - Multiple & raised. Above the surface
 - Undermined edges & necrotic floor.
 - In the small intestine they are oval with their longitudinal axis parallel to that of intestine.
 - In the large intestine the ulcers are rounded.
 - 4-During the 4th & 5th weeks: the ulcers heal with minimal scar.
 - 5-The mesenteric lymph nodes are enlarged and show hyperplastic follicles and macrophages.

Extra intestinal lesions:

- 1-Spleen: Acute splenic swelling:
 - Gross: moderate enlargement with dark soft focally necrotic red pulp.
 - Microscopy: Several macrophages inside splenic sinusoids.
- 2-Bone marrow: Depression of leukocyte formation (leucopenia) except monocytes. the formation of which may be even stimulated (monocytosis).
- 3-Gall bladder may be inflamed (typhoid cholecystitis). A carrier state may develop.
- 4-Toxic (degenerative) lesions
 - Liver, heart and kidney: cloudy swelling and may be fatty change.
 - Veins: toxic thrombophlebitis may occur.
 - Skeletal muscles: Zenker's degeneration (see general pathology)
 - Skin rash may occur.

Complications:

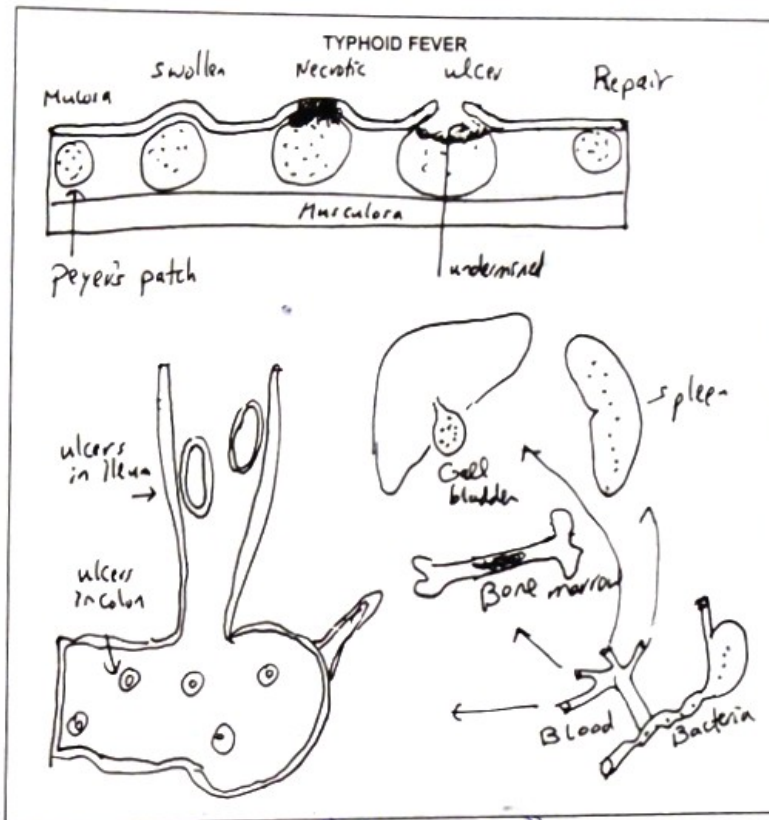
Intestinal complications:

- 1- Hemorrhage.
- 2- Ulcer perforation leading to peritonitis.

Extra intestinal complications:

- 1- Heart failure due to toxic myocarditis & toxic endocarditis.

- 2- Kidney: Pyelonephritis.
- 3-Gall bladder: Cholecystitis (which may lead to carrier state and gall stone formation).
- 4- Lungs: Bronchopneumonia.
- 5- Bones and joints: Osteomyelitis and arthritis.
- 6- Nervous system: Meningitis, encephalitis and neuritis.
- 7- Toxic thrombophlebitis.
- 8-Toxic (degenerative) lesions: see above and describe.



DYSENTERY

Definition: Inflammation of the large intestine characterized by diarrhea & tenesmus, usually accompanied by passage of blood and mucus with stools.

Types: The commonest types are:

- 1) amoebic dysentery
- 2) bacillary dysentery
- 3) bilharzial dysentery.

* what is definition?
= what is characteristic
of dysentery?

Dysentery
GIT

Comparison

Large intestine function
absorption of water
from waste product

Engleberg Descenty 38,
 ↳ Actiology
 ① Co = Coarctation
 ② MT = Meckel's diverticulum
 ③ PF = Pyloric Fistula

10/15
 * Definition of dysentery + Caused by ---

MT =

AMOEBIIC DYSENTERY	BACILLARY DYSENTERY
AETIOLOGY AND PATHOGENESIS	AETIOLOGY AND PATHOGENESIS
Ingestion of food contaminated with <i>Entamoeba histolytica</i> cysts. The cyst wall is dissolved in the small intestine (due to alkalinity) → 4 amoebae → division & invasion of mucosa (mainly colonic mucosa) aided by their proteolytic enzymes. <i>phagocytosis</i> Remark: Lesions are mainly produced in colon because foecal stagnation allows amoeba to invade.	Ingestion of food contaminated with <i>Shigella</i> bacilli. These bacteria secrete powerful exotoxins leading to pseudomembranous inflammation. <i>exotoxin</i> Remark: The colon is mainly affected.

GROSS FEATURES

Colonic amoebic ulcers:

- Multiple.
- Small or large.
- Deep undermined edges (flask shaped ulcers).
- Floor: Yellowish necrotic.
- Base: Formed of musculosa.
- Mucosa in between the ulcers is normal.
- Healing (fibrosis) may cause intestinal stricture.

Colonic pseudomembranous inflammation.

Parts of the mucosal necrotic false membrane detach leading to small superficial ulcers with sharp edges. The intestinal lumen contains greenish exudate and the mesenteric nodes are enlarged.

MICROSCOPY

The edges and floor of ulcers show amoebae surrounded by clear zones due to lysis of the surrounding tissues by the proteolytic enzymes of the amoebae. The amoebae are rounded, 25 microns in diameter with eccentric nuclei. Necrotic foci and few inflammatory cells surround the amoebae.

- 1-The pseudomembrane consists of necrotic mucosa, fibrin, PMNs, macrophages and bacteria.
- 2-Submucosa: Dilated capillaries, neutrophils, macrophages, fibrin....

COMPLICATIONS of ulcers + specific complications

A) INTESTINAL COMPLICATIONS:

- 1-Haemorrhage.
- 2-Perforation leading to septic peritonitis.
- 3-Rectal prolapse due to straining.
- 4-Intussusception due to abnormal peristalsis.
- 5-Intestinal stricture (fibrosis).
- 6-Amoeboma: It is amoebic granuloma together with secondary infection forming a large mass.
- 7-Chronic carrier.

B) SPREAD OF INFECTION:

- Direct → perianal skin ulcer.
- Blood → amoebic liver abscess and sometimes amoebic abscess of lung and brain.

A) INTESTINAL COMPLICATIONS:

- 1-Haemorrhage.
- 2-Perforation leading to septic peritonitis.
- 3-Rectal prolapse.
- 4-Intussusception due to abnormal peristalsis.
- 5-Intestinal stricture.
- 6-Secondary infection.
- 7-Chronic carrier.

B) TOXAEMIA:

- Toxic myocarditis.
- Arthritis, peripheral neuritis.
- Intus.

AMOEBIIC LIVER ABSCESS:

Aetiology: Spread of amoeba from intestine to liver through the portal vein.

Pathology: The right lobe is more common. Foci of necrosis (amoebic hepatitis) are followed by liquefaction and formation of amoebic abscess characterized by:

Gross:

- Abscess may be single or multiple.
- Usually large.
- Irregular shaggy wall.
- Lumen contains chocolate coloured fluid (called amoebic pus).

Microscopy:

- Amoebic pus: necrotic liver tissue.
- Wall of abscess contains amoebae and inflammatory cells.

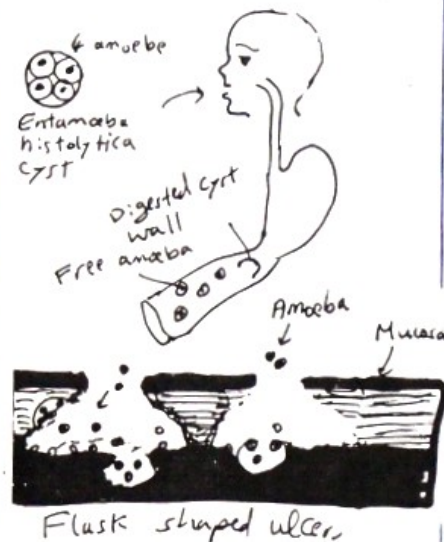
Examine what complication of Amoebic + discuss one? *Amoebic Liver Abscess*

Amoeboma
 not a tumour at all
 so it's not benign
 not malignant → It's Amoebic granuloma

Complications:

- 1-Secondary infection leads to pus formation and toxemia.
- 2-Compression of the bile ducts leads to jaundice.
- 3-Rupture: a) upwards this leads to lung abscess. b) downwards to peritoneum.
- 4-Spread of amoebae through hepatic veins to lungs then to systemic circulation.
- 5-Chronicity: The abscess wall becomes fibrotic and may be calcified.

AMOEBIIC DYSENTERY



BACILLARY DYSENTERY



discuss one of Abscess
 Amoebic Liver abscess
 human
 not in of pus like abscess

ACUTE APPENDICITIS (A)

Aetiology:

1-Causative bacteria: Streptococci, E. coli, Staphylococci.

2-Route: Most commonly from lumen of intestine.

3-Appendicular obstruction

It is an important predisposing factor since it leads to retention of appendicular mucus in the lumen → pressure on mucosal vessels → mucosal ischemia → facilitation of bacterial invasion.

Appendicular obstruction may be due to:

- In the lumen: Seeds of plants or fruits or faecolith.
- In the wall: Fibrosis or lymphoid hyperplasia.
- Outside the wall: Peritoneal adhesions.

Pathology:

1-Acute catarrhal appendicitis: This is the mildest type:

Gross: Appendix is congested and slightly swollen.

Microscopy: Catarrhal inflammation.

Fate:

- May resolve.
- May progress to suppurative appendicitis.

2-Suppurative appendicitis:

Gross: Appendix is congested and swollen. Lumen contains pus. Mucosa is ulcerated. Serosa shows exudate. Appendicular mass may occur (see complications; describe)

Microscopy:

- Necrotic mucosa.
- The whole wall shows dilated capillaries, PMNs, pus cells, macrophages...etc.

Fate: If not excised (appendectomy) it may become complicated.

3-Acute gangrenous appendicitis: see complications.

Complications:

1-Acute Gangrenous Appendicitis:

Severe suppurative appendicitis may be followed by putrefaction → gangrene, perforation & peritonitis → severe toxemia

2-Appendicular Mass And Abscess:

In some cases of acute suppurative appendicitis, the appendix may become glued by fibrinous exudate to the adjacent intestinal loops and to the greater omentum (policeman of the abdomen) producing appendicular mass. Inflammation may resolve or suppuration progresses → appendicular abscess.

Fate of appendicular abscess: May resolve or become complicated by:

a) Rupture:

- Into peritoneal cavity → diffuse peritonitis.
- Into abdominal wall → sinus or into loops of intestine → fistulae.

b) Healing leads to peritoneal adhesions which may cause intestinal obstruction.

3-Rupture and septic peritonitis.

4-Portal Pyaemia (due to thrombophlebitis of appendicular vein).

5-Chronic Appendicitis in which fibrosis may cause stenosis of the appendicular lumen (chronic obliterative appendicitis) leading to repeated acute attacks.

6-Mucocele Of Appendix: Catarrhal appendicitis in the presence of appendicular obstruction causes distension of appendix with mucus (mucocele). Fate of mucocele:

- Rupture into peritoneal cavity leading to pseudomyxoma peritonii.
- 2ry infection leading to empyema of the appendix.

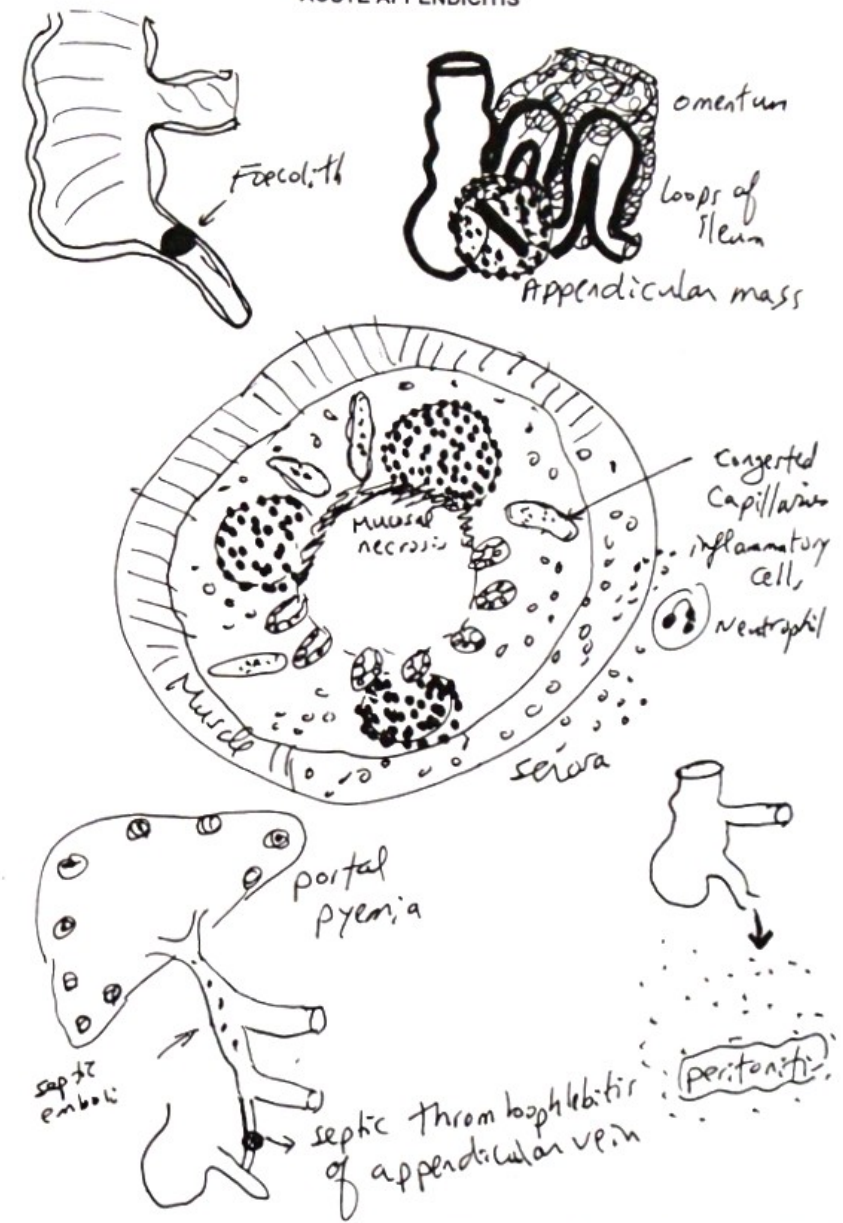
@ pathology
 @ catarrhal
 @ suppurative
 @ gangrenous
 = pathology complication

*acute appendicitis or abscess always appendectomy

rupture diffuse peritonitis
 heal → obst

false tumor in peritonium

ACUTE APPENDICITIS



IDIOPATHIC INFLAMMATORY BOWEL DISEASE (IBD)

I- ULCERATIVE COLITIS

Definition: Chronic inflammatory disease of unknown aetiology affecting the mucosa of any part of the colon. It is characterized by active phase of inflammation of the colon, manifested clinically by attacks of abdominal pain, diarrhea and bleeding. These active phases are separated by periods of remissions. This disease progresses & becomes chronic.

Aetiology:

Unknown. However autoimmune, psychosomatic & genetic factors are suspected.

Gross: The disease usually starts in the rectum (ulcerative proctitis), but may progress to involve the whole colon (ulcerative pancolitis). Affected parts show:

- 1- Congested friable mucosa, easily bleeding on touch
- 2- Multiple superficial irregular ulcers are common during the active disease phase.
- 3- The mucosa between the ulcers may show pseudopolyps (in chronic phase of the disease).
- 4- Fibrosis may occur in prolonged chronic cases.

Microscopy:

1- The active phase of the disease is characterized by:

- a) Mucosal ulcers.
- b) Crypt abscesses (crypt lumens contain neutrophils and pus cells).
- c) The lamina propria shows congested capillaries many neutrophils & mononuclear leucocytes.

* * d) Goblet cell depletion.

2- Chronic phase of the disease is characterized by:

- a) Crypt branching
- b) Pseudopolyps: Swollen oedematous congested inflamed hyperplastic mucosa
- c) Mucosal dysplasia may develop in prolonged cases.
- d) Fibrosis.

Complications:

- 1- Haemorrhage.
- 2- Perforation (septic peritonitis)
- 3- Fistula.
- 4- Precancerous leading to carcinoma (30% of cases after 30 years).
- 5- Stricture of colon.
- 6- 2ry amyloidosis.
- 7- Liver damage of unknown mechanism: Steatosis, biliary cirrhosis....

II- REGIONAL ENTERITIS (CROHN'S DISEASE)

Definition: Chronic inflammatory disease of unknown aetiology affecting any part of the gut from mouth to anus, but most commonly the terminal ileum. It is characterized by transmural inflammation of the affected part (whole wall inflammation, not restricted to mucosa), manifested clinically by attacks of abdominal pain, malabsorption & loss of weight.

Aetiology:

Unknown. Autoimmune, psychosomatic, genetic or infective factors may be involved.

Gross: Terminal ileum (or less commonly jejunum, colon, stomach) show:

- 1- Mucosal fissures with intervening free areas (skip areas).
- 2- Enlarged mesenteric nodes.
- 3- Rigid wall due to fibrosis.
- 4- Congested mesentery.

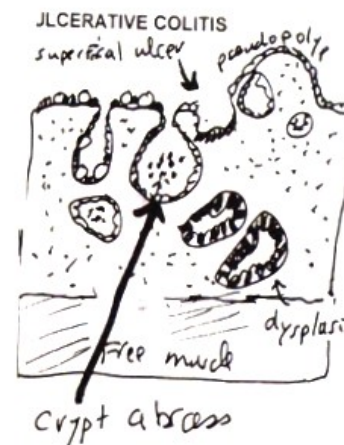
Microscopy:

- 1- Chronic nonspecific inflammation, associated in 60% of cases with non-caseating sarcoid-like granulomas (epithelioid cells, giant cells).
- 2- Inflammation is transmural (affecting the full thickness of wall).
- 3- Later fibrosis occurs.

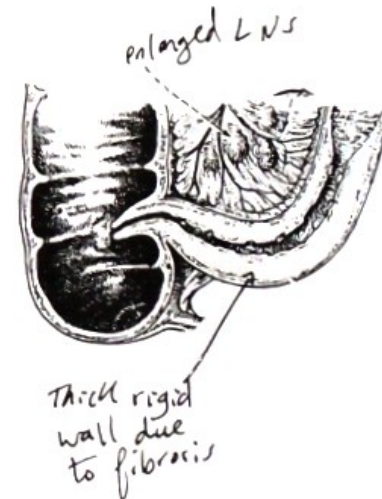
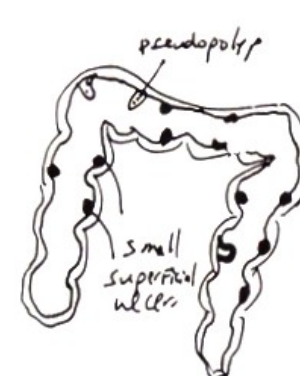
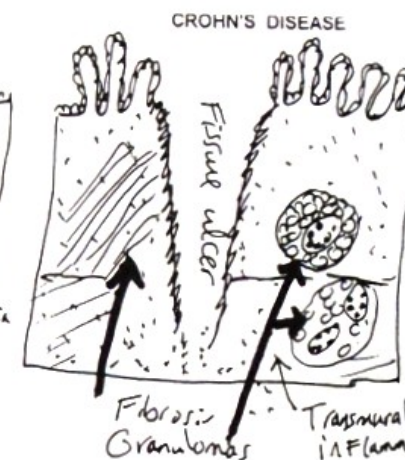
Complications:

- 1- Haemorrhage.
- 2- Perforation and development of fistulae.
- 3- Malabsorption.
- 4- Intestinal stricture.
- 5- Amyloidosis.
- 6- Rarely carcinoma of small or large intestine

ULCERATIVE COLITIS



CROHN'S DISEASE



DIVERTICULA OF INTESTINE

DEFINITION: Diverticula are intestinal pouches

TYPES:

1- **Congenital diverticula**: Consist of all layers of intestinal wall. These may occur in caecum or duodenum, but the most common is Meckel's diverticulum (ileum).

2- **Acquired diverticula**: Consist of mucosa & submucosa projecting through defects in musculosa.

Meckel's Diverticulum: It is the commonest type of congenital diverticula.

- It is due to failure of obliteration of the proximal part of the vitello-intestinal duct.
- It exists in 2-3% of people. It is 2-3 inches long. It exists at the anti-mesenteric border of intestine, 2-3 feet from the ileocaecal valve. Its wall consists of all intestinal layers, but may contain ectopic gastric mucosal tissue or pancreatic tissue.

Complications occur in 2-3% of cases and include:

- 1- Diverticulitis (same aetiology as appendicitis).
- 2- Peptic ulcer.
- 3- Volvulus and intussusception.

Acquired Diverticula:

These are multiple mucosal (& submucosal) outpouches (diverticulosis)

Sites:

- 1- Rarely small intestine: duodenum, jejunum or ileum (at the mesenteric border).
- 2- Commonly colon "Diverticular Disease Of Colon", particularly left sided, at mesenteric side

Aetiology:

- 1- Senile weakness (atrophy) of intestinal wall.
- 2- Rise of intracolonic pressure due to constipation.

Pathology:

- 1- Mucosal/submucosal herniation through muscle defects, usually at sites of entry of vessels.
- 2- Diverticula are multiple (diverticulosis) & small, seen at the mesenteric side.
- 3- Small intestinal diverticula contain fluid chyme, colonic diverticula contain fecal material

Complications:

- 1- Diverticulitis may produce abscess
- 2- Perforation → septic peritonitis.
- 3- Fistulae.
- 4- Intestinal hemorrhage.
- 5- Fibrous stricture.

HERNIA

Definition: It is protrusion of a part of a viscous (usually an intestinal loop) through a congenital or acquired defect in the wall of the cavity in which the viscous exists.

Aetiology:

- 1- The defect may be congenital or acquired (e.g. weak scar following surgery).
- 2- Rise of intra-abdominal pressure (coughing, lifting heavy weights, large abdominal tumors, pregnancy..)

Types:

- 1- Internal hernia as hiatus hernia
- 2- External hernia as femoral, inguinal, umbilical and postoperative incisional hernia.

Complications:

- 1- Irreducibility.
- 2- Inflammation.
- 3- Obstruction.
- 4- Strangulated hernia:

Causes:

- a) Distension of the hernial intestinal loop by excess contents → constriction (strangulation) of the loop against the edges of the defect.
- b) Crowding of the hernial sac by herniation of a new loop of intestine or omentum.

Effects: Strangulation leads to:

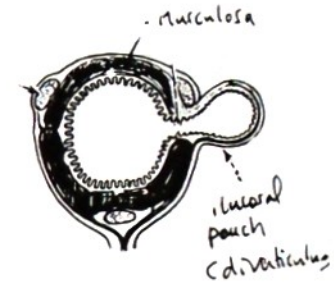
a) Local effects:

- Compression of veins on the intestinal wall → congestion & oedema
- Compression of arteries → intestinal infarction and moist gangrene.
- Leakage of intestinal contents through gangrenous loop → peritonitis & toxemia.
- Intestinal collapse distal to obstruction & dilatation proximal to obstruction.

b) **General effects:** Vomiting, dehydration, shock & electrolyte imbalance

MECKLE'S DIVERTICULUM

COLONIC DIVERTICULAR DISEASE



HERNIA



Meckel's Diverticulum Acquired Diverticulum

INTESTINAL OBSTRUCTION

1) ACUTE INTESTINAL OBSTRUCTION

DEFINITION:

This is sudden complete obstruction. Usually small intestinal.

TYPES:

- 1-Functional obstruction (paralytic ileus)
- 2-Organic obstruction:
 - a) simple obstruction
 - b) strangulated obstruction
 - c) obstruction due to mesenteric vascular occlusion

FUNCTIONAL OBSTRUCTION = PARALYTIC ILEUS:

Definition: This is sudden loss of intestinal peristalsis.

Aetiology: Sudden neuromuscular (autonomic) dysfunction caused by

- a) sympathetic stimulation during abdominal operations
- b) parasympathetic inhibition as by toxins in cases of peritonitis.
- c) Spinal cord injuries.

Effects:

- a) General effects: Vomiting, dehydration, shock & electrolyte imbalance
- b) Local effects: Intestinal dilatation due to loss of peristalsis

ORGANIC OBSTRUCTION:

A) SIMPLE OBSTRUCTION:

Definition: Obstruction of the lumen of intestine without occlusion of mesenteric vessels

Aetiology:

- a) mass of ascaris worms
- b) swallowed foreign body
- c) faecal concretion on top of chronic intestinal obstruction (see below)
- d) gall stone ileus (see gall stones).

Effects:

- a) General effects: Vomiting, dehydration, shock & electrolyte imbalance
- b) Local effects:

- Intestinal collapse distal to obstruction.
- Intestinal distention (fluids & gases) proximal to obstruction, associated with strong peristalsis.
- Venous compression due to intestinal distention → oedema & hemorrhage
- Bacteria may penetrate the intestinal wall producing peritonitis.

B) VASCULAR OBSTRUCTION (mesenteric vascular occlusion)

Definition & aetiology: Thrombosis or embolism of mesenteric vessels leads intestinal gangrene of the affected intestinal segment with loss of peristalsis (intestinal obstruction). Mesenteric artery thrombosis is usually on top of atherosclerosis. Embolism may be derived from cardiac thrombi as vegetations.

Effects:

- a) General effects: Vomiting, dehydration, shock & electrolyte imbalance
- b) Local effects:

- Hemorrhagic infarction & intestinal gangrene → toxemia, rupture & peritonitis.
- Intestinal collapse distal to obstruction.
- Intestinal distention (with fluids and gases) proximal to obstruction.
- Venous compression due to intestinal distention → intestinal oedema & hemorrhage

C) STRANGULATED OBSTRUCTION:

Definition: This is simultaneous obstruction of intestine & mesenteric vessels

Types:

- Intussusception.
- Volvulus.
- Strangulated hernia.

INTUSSUSCEPTION:

Definition: Invagination of an intestinal segment (intussusceptum) into a distal segment (intussusceptum). The intussuscepted bowel may be palpable as a sausage-shaped mass in the abdomen.

Aetiology: Most common in infants. Due to irregular peristalsis:

- Gastroenteritis.
- Intestinal parasites.
- Meckel's diverticulum.
- Intestinal tumors or polyps.
- Irritant food, fasting....

Types:

- a- Ileocaecal intussusception: Commonest type.
- b- Enteric (Ileo-ileal).
- c- Colonic (Colo-colonic): Rare.

Effects:

- a) General effects: Vomiting, dehydration, shock & electrolyte imbalance
- b) Local effects:

- Hemorrhagic infarction & intestinal gangrene → toxemia, rupture & peritonitis.
- Intestinal collapse distal to obstruction.
- Intestinal distention (with fluids and gases) proximal to obstruction.
- Venous compression due to intestinal distention → intestinal oedema & hemorrhage

VOLVULUS:

Definition: Twisting of a loop of intestine upon itself about the axis of its mesentery or around an abnormal fibrous band.

Aetiology:

- a) Volvulus of sigmoid (commonest) may occur in patients with congenital long mesocolon & loaded sigmoid due to constipation.
- b) Volvulus of ileum may rarely occur in cases of Meckel's diverticulum.

Effects:

- a) General effects: Vomiting, dehydration, shock & electrolyte imbalance
- b) Local effects:

- Hemorrhagic infarction & intestinal gangrene → toxemia, rupture & peritonitis.
- Intestinal collapse distal to obstruction.
- Intestinal distention (with fluids and gases) proximal to obstruction.
- Venous compression due to intestinal distention → intestinal oedema & hemorrhage

STRANGULATED HERNIA: See before & describe.

GENERAL EFFECTS OF ACUTE INTESTINAL OBSTRUCTION:

- 1- Repeated attacks of vomiting lead to:
 - a) Dehydration and Shock.
 - b) Potassium loss leads to myocardial damage.
- 2- Toxaemia occurs in cases complicated by peritonitis

LOCAL EFFECTS OF ACUTE INTESTINAL OBSTRUCTION :

1- Acute Intestinal Obstruction without vascular affection

(paralytic ileus & simple obstruction) :

- Intestinal collapse distal to obstruction.
- Intestinal distention (with fluids and gases) proximal to obstruction, associated with strong peristalsis (except in paralytic ileus).
- Venous compression due to intestinal distention → oedema & hemorrhage.
- Bacteria may penetrate the intestinal wall producing peritonitis.

2- Acute Intestinal Obstruction associated with vascular occlusion (mesenteric occlusion and strangulated cases i.e. intussusception, volvulus...etc) : The effects are similar to those described above, but more over intestinal gangrene occurs leading to severe toxemia, intestinal hemorrhage and peritonitis. Mortality is high.

(A) II) CHRONIC INTESTINAL OBSTRUCTION

DEFINITION: This is gradual incomplete obstruction. It usually occurs in the large intestine.

AETIOLOGY :

1- Fibrous stricture following dysentery, ulcerative colitis, Crohn's disease, diverticulosis, TB ...

2- Tumors.

3- Peritoneal adhesions.

4- Megacolon: a) Congenital type (Hirschsprung's disease). b) Acquired (Idiopathic) type.

PATHOLOGY AND EFFECTS :

1- Distal to obstruction some degree of intestinal collapse, occurs.

2- Proximal to obstruction : Intestinal hypertrophy and dilatation, the mucosa shows stercoral ulcers (caused by trauma of the retained faeces).

3- Constipation.

4- Vomiting (less frequent than in acute obstruction).

5- The retained faeces may become hard (faecal concretion) and may become impacted in the narrow intestinal segment leading to acute intestinal obstruction.

Hirschsprung's disease (Congenital Megacolon):

Aetiology: It is a disease of children characterized by congenital absence of ganglion cells in the myenteric and submucosal plexuses of the colon mainly at the anorectal junction

Effects:

1- Block of peristalsis at the aganglionic segment → chronic intestinal obstruction

2- Marked hypertrophy and dilatation of the colon (megacolon) proximally.

3- Abdominal distension & constipation.

MALABSORPTION SYNDROMES

DEFINITION: Small bowel disease characterized by defective absorption of proteins, carbohydrates, fats, vitamins & others. Some types start at infancy, others in children or adults.

EFFECTS:

1- Chronic diarrhea and failure of infants to thrive

2- Loss of weight, anemia, vitamin deficiency.

3- Muscle, nervous, endocrine and immunological defects due to chronic malnutrition state

TYPES:

1- Celiac Disease (Gluten-induced enteropathy): It is characterized by:

- Total villous atrophy. The small bowel mucosa appears flat.
- Marked improvement when the wheat protein (gluten) is removed from diet.
- Autoimmune (antigliadin and other autoantibodies exist in patient's serum).
- Intestinal lymphoma is a rare complication.

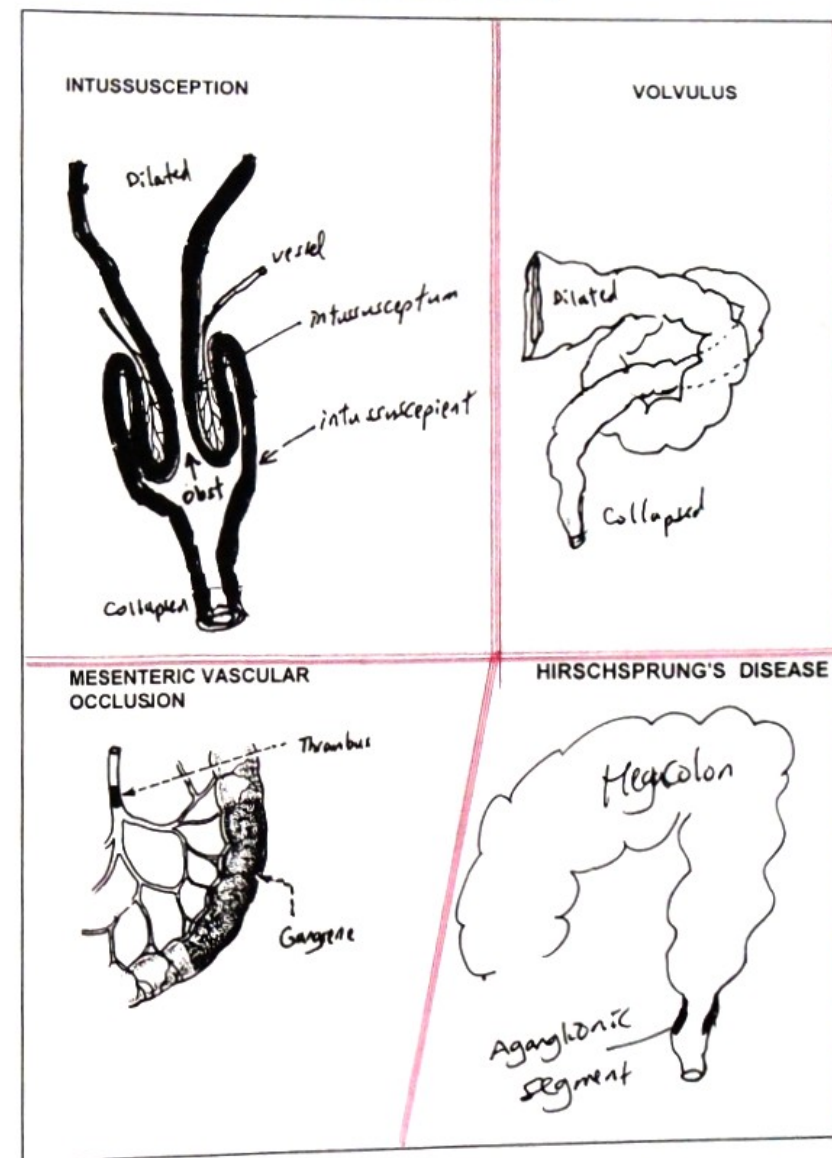
2- Tropical Sprue: It is characterized by:

- Partial villous atrophy.
- Unaffected by gluten ingestion.

• Thought to result from chronic bacterial infection.

3- Whipple's Disease: It is characterized by distension of the villi and lamina propria by a large number of large pale macrophages (foamy histiocytes) containing large numbers of bacilli.

4- Intestinal Amyloidosis, Crohn's Disease And Others





TUMORS OF SMALL & LARGE INTESTINE

BENIGN TUMORS :

- ADENOMAS (polypoid adenomas):** More common in colon. They include :
 - 1-Tubular Adenoma (Adenomatous Polyp):** Solitary or multiple. It consists of proliferating tubular glands that show dysplasia. Commonest in rectum. Precancerous.
 - 2-Villous Adenoma (Papillary Adenoma):** It is often solitary. It consists of branching glands showing dysplasia. Commonest in rectum. Precancerous.
 - 3-Tubulovillous Adenoma:** It shows combined features of the above two types.
 - 4-Familial Polyposis:** A hereditary (autosomal dominant) disease. The entire colon shows hundreds of small polyps of the mixed tubulo-villous type. It is highly precancerous and malignant change (polyposis carcinoma) occurs around the age of 30 years.
- Polyposis Syndromes:** Several polyposis syndromes are well documented e.g. **Gardner's syndrome** (colonic polyps, osteomas and exostosis) & **Turcot's syndrome** (colonic polyps and brain tumors).
- Hamartomatous Polypi (Peutz-Jegher's Syndrome):** *Not tumors but it's tumours like*
 A hereditary (autosomal dominant) disease characterized by:
 - Multiple gastrointestinal polyp composed of mucous glands, fibrous cores, smooth muscle bundles (hamartoma).
 - Melanin pigmentation of face, lips, oral mucosa and digits.
- Other benign tumors:**
 GIST, Leiomyoma, fibroma, hemangioma, Schwannoma, neurofibroma, Lipoma.

MALIGNANT TUMORS

- 1-Adenocarcinoma (more common in colon).
- 2-Malignant lymphoma (more common in small intestine).
- 3-Carcinoid (more common in small intestine and appendix).
- 4-GIST and Sarcomas:

(X) BENIGN & MALIGNANT TUMORS OF APPENDIX: Rare

MALIGNANT:

- 1)The most common appendicular tumor is carcinoid
- 2) Rarely adenocarcinoma, lymphoma

BENIGN (as those of intestine) are extremely rare in appendix.

CARCINOMA OF LARGE INTESTINE

A common tumor. Relatively more common in males. ♂

Age:

- Usually above 45 years.
- May occur in younger ages (around or below 30 years) on top of familial polyposis.

Predisposing factors:

- Increased dietary fat.
- Decreased dietary fiber.
- Familial polyposis, tubular adenoma, villous adenoma.
- Dysplasia of ulcerative colitis

Sites:

- 1)75% in rectum and sigmoid.
- 2)25% in the rest of colon (caecum, ascending....).

Gross:

- One of the following:
- 1-A polypoid mass fungating into the lumen.
 - 2-An irregular malignant ulcer with everted edges, necrotic floor and indurated base.
 - 3-An infiltrating growth that may lead to stricture of a segment of intestine (annular type).

Microscopy:

- 1-Adenocarcinoma; Commonest. (describe from general pathology).
- 2-Mucoid carcinoma (describe) or Signet ring cell carcinoma (describe)
- 3-Undifferentiated carcinoma (Scirrhus carcinoma ...describe).

Spread:

- 1-Direct: To urinary bladder, vagina (fistulae may form), liver ...etc.
- 2-Lymphatic: To mesenteric and paraortic lymph nodes.
- 3-Blood: To liver then lungs and other sites.
- 4-Transcoelomic: Lead to hemorrhagic ascites and peritoneal metastatic masses. Krukenberg tumors may occur in females.

Other effects:

- 1-Bleeding per rectum
- 2- Piles
- 3-Intestinal obstruction
- 4- Intestinal perforation producing septic peritonitis.
- 5--Fistula between intestinal loops, bladder, vagina...

Staging Systems of Cancer Colon:

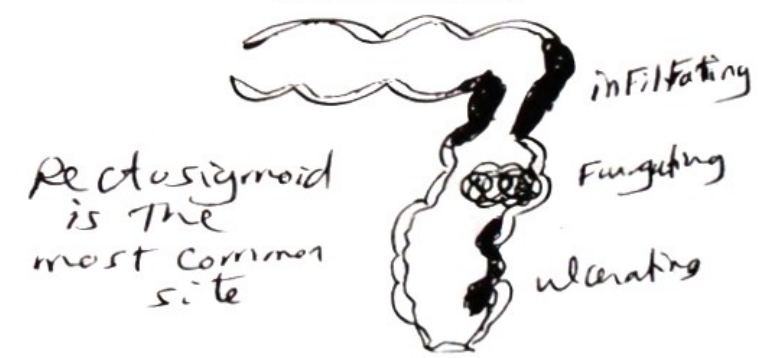
1-T.N.M. Staging:

Tis: Carcinoma in situ.	N0: No lymph node metastases.	M0: No distant metastases.
T1: Tumor invades till submucosa.	N1: Metastases in 3 pericolic or perirectal nodes	M1: Distant metastases.
T2: Muscularis invaded.	N2: Metastases in 4 or more pericolic or perirectal nodes	
T3: Subserosa invaded.	N3: Metastases in any nodes along the course of major blood vessels.	
T4: Tumor invades visceral peritoneum & may involve nearby tissues or organs.		

2-Modified Duke's Staging:

- Stage A: corresponds to T1, N0, M0
 Stage B1: corresponds to T2, N0, M0
 Stage B2: corresponds to T3 or T4, N0, M0
 Stage C1: corresponds to T1 or T2, N1,2 or 3, M0
 Stage C2: corresponds to T3 or T4, N1,2 or 3, M0
 Stage D: corresponds to any T, any M, M1

COLONIC CARCINOMA



CARCINOID TUMOR (ARGENTAFFINOMA)

Arises from argentaffin (neuroendocrine) cells of ileum, appendix or any other part of gut.

Gross: A firm yellowish submucosal nodule, or multiple nodules.

Microscopy: Groups of small polyhedral cells with cytoplasmic argyrophilic granules (stainable with silver). The cells are usually monotonous (monomorphic).

Behavior: The tumor is locally malignant, or malignant. Malignant carcinoid metastasizes to liver leading to **Carcinoid Syndrome** (caused by unmetabolized serotonin & other substances released from liver metastases). Carcinoid syndrome is manifested by:

- 1-Fibrous stenosis of tricuspid and pulmonary valves.
- 2-Bronchospasm (asthma-like attacks occur).
- 3-Skin flushing, oedema, diarrhea.

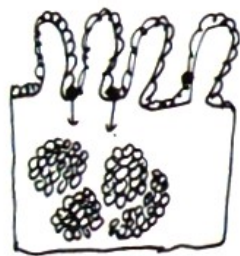
Mechanism of Carcinoid Syndrome: (X)

• Serotonin & other substances produced by the argentaffin cells of the normal GIT mucosa or by cells of the carcinoid tumors are inactivated in the liver by the enzyme monoamine oxidase. Therefore these substances do not reach the systemic veins.

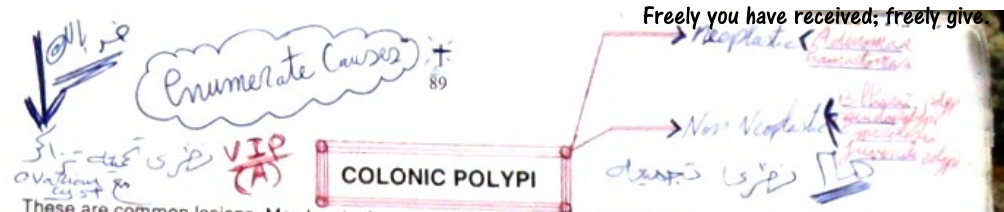
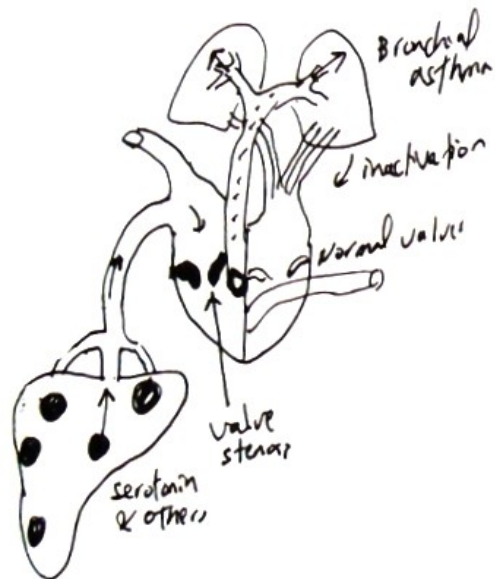
• With carcinoid liver metastases, serotonin, histamine, kinins, prostaglandins, neuropeptide K & substance secreted by tumor cells → systemic veins → **carcinoid syndrome**:

- 1-When these substances reach the right side of the heart, tachykinins (and probably serotonin) → injury and fibroblastic proliferation of the valves of the right side.
- 2-Then these substances reach the lung → bronchospasm. Most of these substances are inactivated in the lung (by the monoamine oxidase enzyme) and therefore they reach the left side, mostly in inactive state → no left side valve lesions (except in very rare occasions).
- 3-Some of the substances passing from the left side to systemic circulation (probably incompletely inactivated) cause skin flushing and diarrhea.
- 4-Carcinoids arising outside the GIT → carcinoid syndrome in absence of liver metastases.

CARCINOID TUMOR



CARCINOID SYNDROME



COLONIC POLYPI

These are common lesions. May be single or multiple. May be non-neoplastic or neoplastic.

NON-NEOPLASTIC POLYPI (2) all non-pneumatous except pseudopolyp (ulcerated)

1-Bilharzial Polyp (see general pathology).

2-Pseudopolyp (see ulcerative colitis).

3-Hyperplastic Polyp: Consist of hyperplastic mucosal glands showing excess mucin secretion. They are very common in the colon and appear as small sessile polyps. } due to irritation

4-Juvenile Polyp: (retention polyp): Occur in children mainly in the rectum and consist of hyperplastic glands of which some are cystically dilated with mucin.

NEOPLASTIC POLYPI (2)

1-Adenomas (polypoid adenomas): → 86 cases / 100

Tubular adenoma, villous adenoma, tubulo-villous adenoma, familial polyposis → describe

2-Hamartomatous polyps. = Peutz-Jeghers syndrome - not tumour

BLEEDING PER RECTUM

Def: Passage of red blood in stools may be due to:

1-Intestinal Lesions as Local Causes: Traumatic (colitis), Tumors, Anal fissure, Inflammations (bilharziasis, T.B., dysentery, ulcerative colitis...etc).

Idiopathic: Solitary Rectal Ulcer Syndrome

2-General Causes as purpura, leukemia, vitamin C or K deficiency.

PILE (HAEMORRHOIDS): (X) على البواسير

This is varicosity of hemorrhoidal veins of lower end of rectum.

Types:

1-Internal piles: Varicosity of superior hemorrhoidal veins.

2-External piles: Varicosity of inferior hemorrhoidal veins.

Aetiology:

1-Congenital weakness of the hemorrhoidal veins.

2-Portal obstruction due to cirrhosis or bilharzial fibrosis.

3-Central obstruction due to right sided heart failure.

4-Local obstruction due to cancer rectum.

Complications:

1-Haemorrhage and anaemia.

2-Thrombosis.

3-Prolapse and strangulation of piles.

4-Infection and pyaemia.

MELENA

This is passage of dark altered blood with stools due to bleeding from above the duodenum. Therefore, causes of melena are the same as those of haematemesis (describe)

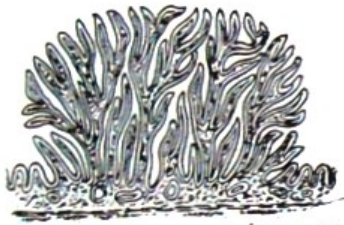
(P. 65)
T.B
VIP

White tongue

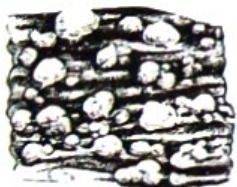
COLONIC POLYPI



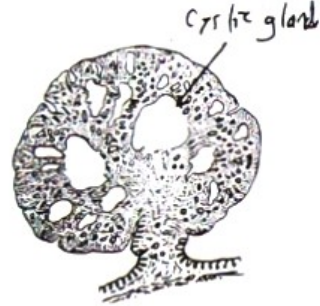
Tubular Adenoma



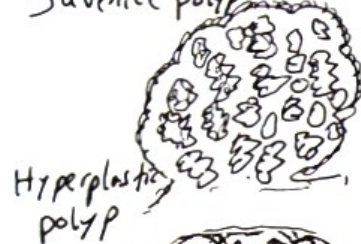
Villous Adenoma



Part of Colon showing Familial polyposis



Juvenile polyp



Hyperplastic polyp



Bilharzial polyp



Hamartomatous polyp

largest organ = skin
largest solid organ = liver - 1/4 lobes
Bile ducts
portal vein
classical triad

CHAPTER VI

DISEASES OF THE LIVER

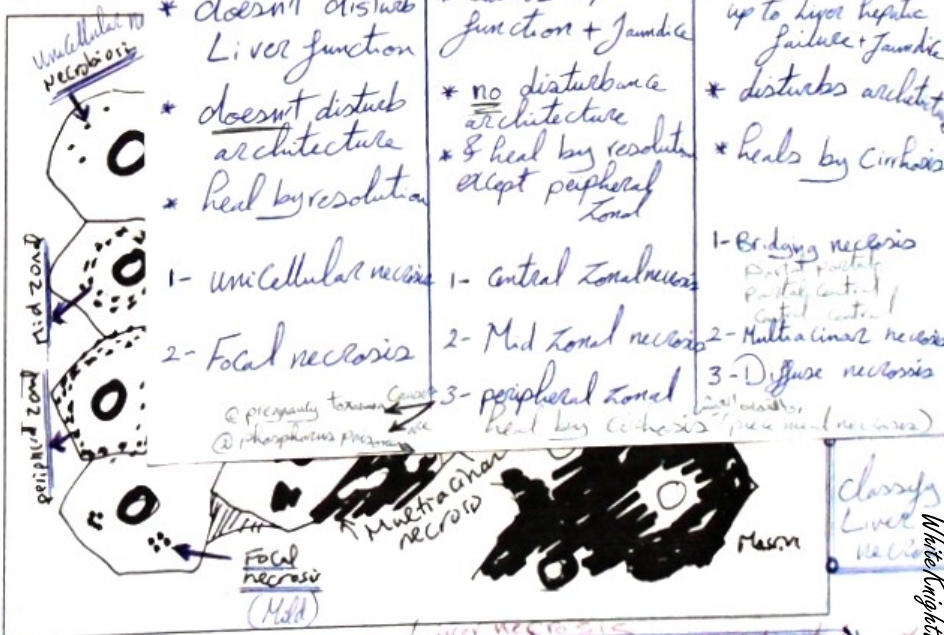
LIVER NECROSIS

Liver necrosis is common in many liver diseases; the most common of which is hepatitis. The degree of liver necrosis is very importantly correlated with the disease course.

- MILD NECROSIS:** It does not disturb liver functions and does not cause cirrhosis. It may be seen in cases of viral or drug hepatitis as well as in mild cases of bacterial toxemia.
 - 1- **Unicellular necrosis (necrobiosis):** This is necrosis of single scattered liver cells
 - 2- **Focal necrosis** affects scattered small groups of liver cells.
- ZONAL NECROSIS:** It affects a particular zone within each hepatic lobule. It causes impairment of liver functions and jaundice. Resolution is expected in central and midzonal types, but cirrhosis can complicate the peripheral zonal type.
 - 1- **Central zonal necrosis** affects hepatocytes around central veins, e.g. in acute viral hepatitis & chronic venous congestion of liver.
 - 2- **Midzonal necrosis** as in cases of yellow fever.
 - 3- **Peripheral zonal necrosis (piecemeal necrosis):** affects hepatocytes at the limiting plates as in chronic hepatitis.

MARKED & VERY MARKED NECROSIS: Liver functions are markedly disturbed (up to hepatic failure).

Mild Necrosis	Zonal necrosis	Marked Necrosis
* doesn't disturb Liver function * doesn't disturb architecture * heal by resolution	* Causes impairment function + jaundice * no disturbance architecture * & heal by resolution except peripheral zonal	* Causes disturbance up to liver hepatic failure + jaundice * disturbs architecture * heals by cirrhosis
1- unicellular necrosis 2- Focal necrosis	1- central Zonal necrosis 2- Mid Zonal necrosis 3- peripheral Zonal	1- Bridging necrosis 2- Multinodular necrosis 3- Diffuse necrosis



classifies Liver Necrosis



Def viral inflammation of liver

VIRAL HEPATITIS

AETIOLOGY:

1-Hepatitis A Virus (HAV): (infectious)

- Transmitted by ingestion of contaminated food or water (infective hepatitis).
- It causes acute hepatitis which is self-limited. It may rarely lead to fulminating hepatitis, but it does not cause chronic hepatitis or carrier states. The virus is shed in stools.
- The incubation period is 2-6 weeks.

2-Hepatitis B Virus (HBV): (severe)

- Transmitted by blood components as plasma. It can also be transmitted by infected needles as in intravenous drug addicts or by contaminated surgical instruments, dental instruments and shaving razors. Hemodialysis (in uremic patients) and organ transplantation are other possible means of transmission.
- The virus is shed in oropharyngeal secretions, in semen & in menstrual blood, therefore it can be transmitted by kissing and by sexual intercourse.
- Transplacental transmission is also possible.
- Illness may be acute hepatitis, fulminating hepatitis, carrier state or chronic hepatitis.
- The incubation period is long (2-6 months).

3-Hepatitis C Virus (HCV): This virus was formerly termed hepatitis non A non B virus.

- The virus is transmitted in a similar way to HBV.
- It may cause acute hepatitis, fulminating hepatitis or carrier state & in EGYPT it is the most common cause of chronic hepatitis.

4-Hepatitis D Virus (HDV): This virus cannot infect persons unless already infected with HBV.

5-Hepatitis E Virus (HEV):

- Transmitted in a similar way to HAV i.e by the fecal-oral route (contaminated food or drink).
- It causes acute hepatitis.
- The importance of HEV infection is that it is an important cause of fulminating hepatitis in pregnant ladies.

Remark: The term viral hepatitis is used to describe hepatic inflammation caused by one of the above mentioned hepatitis viruses. There are however other viruses that can nonspecifically affect the liver as a part of multisystem affection and is usually in the form of acute self-limiting hepatitis e.g. cytomegaloviral hepatitis or Epstein Barr viral hepatitis.

CLINICOPATHOLOGICAL TYPES:

1-Acute Hepatitis: Most commonly due to HAV, but may be caused by HEV, HBV or HCV.

2-Fulminating Hepatitis: Same causes as acute hepatitis.

3-Chronic Hepatitis: Caused by HBV (+ HDV) or HCV or mixed infection.

4-Chronic carrier: caused by HBV or HCV.

ACUTE VIRAL HEPATITIS

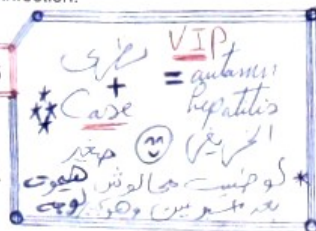
AETIOLOGY: HAV (commonest), HEV, HBV or HCV.

PATHOLOGY:

Gross: Liver is enlarged and yellowish green (bile stained).

Microscopy:

- Hydropic degeneration (ballooning) of hepatocytes.
- Necrosis of hepatocytes: Commonly centrilobular. Necrobiosis and focal necrosis may also occur. Some of the necrotic liver cells appear acidophilic & shrunken (Councilman bodies).
- Inflammatory cells (lymphocytes, macrophages, plasma cells) appear around necrotic cells & in the adjacent portal tracts.
- Cholestasis: This is retention of bile inside the cytoplasm of hepatocytes and inside the bile canaliculi (which are obstructed by the swollen hepatocytes).
- Kupffer cells engulf bile and undergo hyperplasia.
- Framework of the liver is not affected.



CLINICAL PICTURE: Nausea, vomiting, abdominal pain followed by jaundice.

FATE: Termination of acute viral hepatitis may be one of three possibilities:

- Complete recovery in 95% or more of hepatitis A infections.
- Acute fulminating hepatitis: more common with HBV, HCV and HEV (during pregnancy) than HAV (see below and describe).
- Chronic hepatitis or chronic carrier: Not due to hepatitis A or E.

FULMINANT VIRAL HEPATITIS

AETIOLOGY:

It occurs in less than 1% of HAV infections, in 1-4% of HBV infections, 2-5% of HCV infections, in 1-3% of HEV infections of normal persons & in 20-50% of pregnant ladies infected with HEV.

PATHOLOGY: There is severe necrosis which may be massive affecting most of the hepatic parenchyma, or submassive (less severe).

1-Acute Massive Necrosis (Acute Yellow Atrophy):

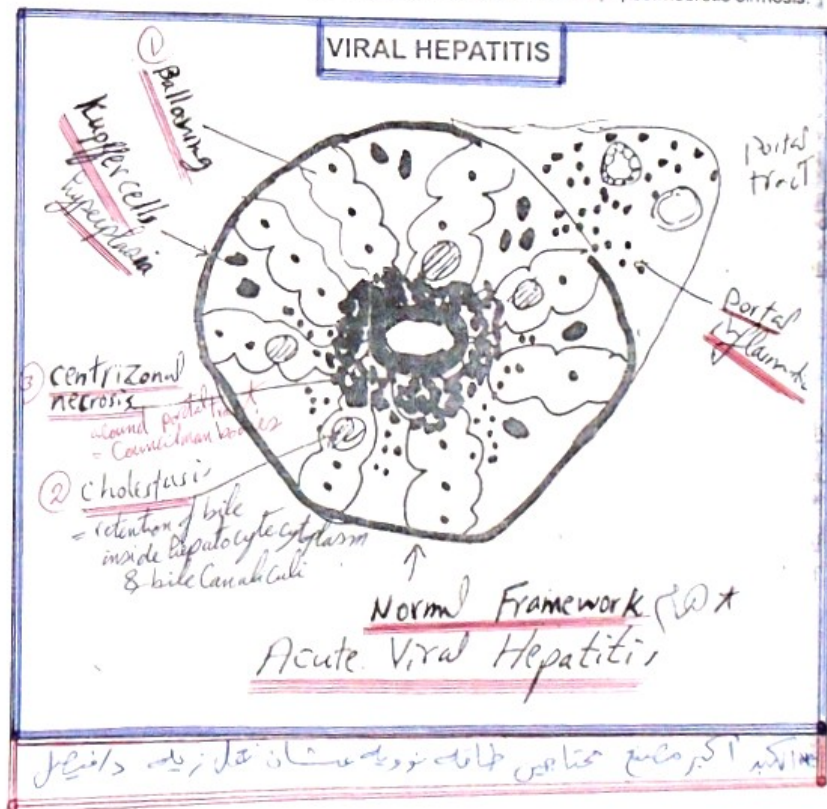
The patient dies in few days due to liver failure.

Gross: Shrunken liver, mottled yellow (necrosis) and red (hemorrhage) areas.

Microscopy: Diffuse liver cell necrosis, sinusoidal rupture, inflammatory cells (lymphocytes, macrophages, plasma cells).

Other pathological features: Necrosis and degeneration of renal tubules and basal ganglia.

2-Subacute Massive Necrosis (Subacute Yellow Atrophy): The patient dies within few weeks from liver failure or may rarely survive longer and develop post-necrotic cirrhosis.



Def viral inflammation of liver

A + stump

VIRAL HEPATITIS

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- Kupfer cells engulf bile and undergo hyperplasia.
- Framework of the liver is not affected.

VIP = acute hepatitis
Case = acute hepatitis
الحالة = acute hepatitis
مريض = acute hepatitis
مرض = acute hepatitis

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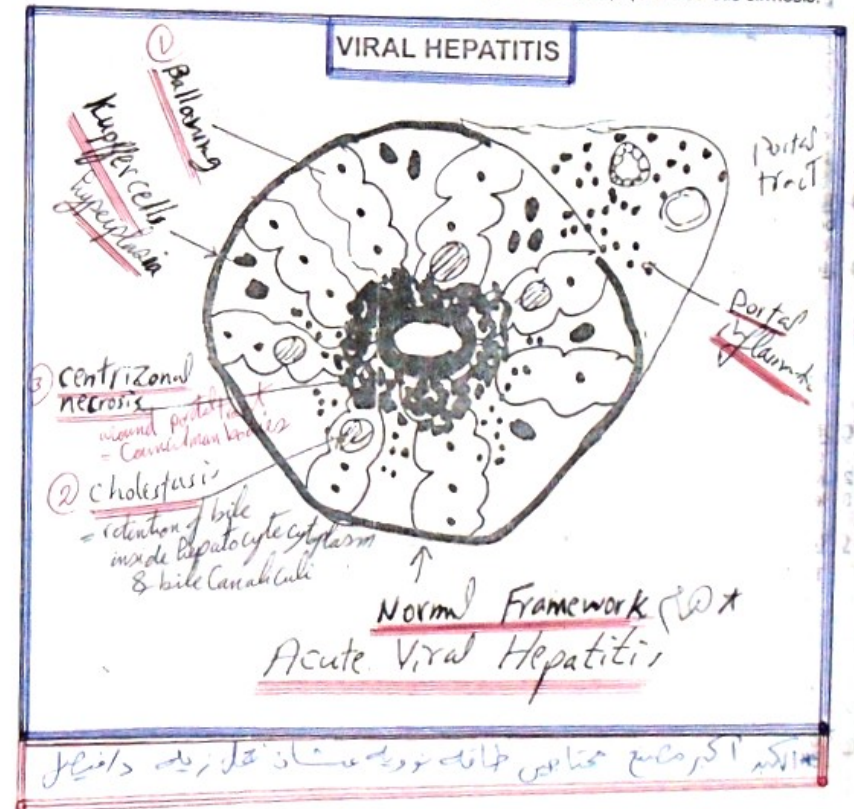
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CHRONIC HEPATITIS

AETIOLOGY:

- Viral aetiology** (most common): HBV (+HDV) or HCV. Mixed infection may occur.
- Autoimmune**: Caused by autoantibodies as antinuclear antibodies & anti-actin antibodies.
- Drug induced**: Isoniazid, methyl dopa, oxyphenisatin and some other drugs.
- Metabolic diseases** as: (a) $\alpha 1$ antitrypsin deficiency (b) Wilson's diseases.
- Cryptogenic** (undetermined aetiology).

CHRONIC VIRAL HEPATITIS

DEFINITION: A chronic 'necro-inflammatory' disease caused by HCV or HBV. The pathological changes start at the interfaces between hepatic lobules and portal tracts, that is why it is referred to as **chronic interface hepatitis**.

GROSS: Usually mild hepatomegaly.

MICROSCOPY:

1-Inflammation (range mild to marked):

- Portal inflammation:** Expansion of the portal tracts by chronic inflammatory cells; mainly lymphocytes. Bile duct walls may be inflamed (mainly in HCV infection).
- Lobular inflammation:** Usually mild.

2-Necrosis (range absent to very marked). It may be:

- Piecemeal necrosis:** This is destruction of the liver cells at the limiting plates of liver lobules (i.e. periportal affecting the parenchymo-mesenchymal interface). The liver cells become detached. Apoptosis may also occur resulting in the formation of apoptotic bodies "acidophilic bodies" which become phagocytized by Kupffer cells. Since piecemeal necrosis occurs at the parenchyma-mesenchymal interfaces (limiting plates), chronic hepatitis was recently termed "chronic interface hepatitis".
- Spotty, bridging or multiacinar necrosis** occur in severe cases.

3-Fibrosis (range absent to very marked; the later is observed when cirrhosis develops). It may be portal fibrosis, bridging fibrosis or bridging fibrosis accompanied by regeneration nodules (cirrhosis).

4-Other Features:

- Ballooning of hepatocytes.
- Steatosis of hepatocytes (mainly in case of hepatitis C).
- Ground glass hepatocytes (in case of hepatitis B).
- Hepatocellular dysplasia (precancerous).
- Cholestasis (in severe cases).

COMPLICATIONS OF CHRONIC HEPATITIS:

- Post hepatic cirrhosis.
- Liver failure.
- Hepatocellular carcinoma. = Hepatoma

GRADING & STAGING OF CHRONIC HEPATITIS:

- There were several trials to score the necroinflammatory activity (grading) of chronic hepatitis as well as the degree of fibrosis (staging). There were several trials (Knodell 1981, Scheuer 1992, modified Scheuer, 2000, Ishak 1995, METAVIR, 1996 and others). In 1995, the International Working Party recommended that diagnosis of chronic hepatitis should include:

1-The aetiology (hepatitis B, hepatitis C...)

2-A scoring system for the grade (degree) of activity $\rightarrow$ 18 = Inflammation Ishak

3-A scoring system for stage of fibrosis $\rightarrow$ 6

- The most popular grading & staging systems are those of Ishak (American) & METAVIR (French).
- Grading & staging correlate with prognosis and response to interferon therapy.

Ishak Activity Scoring System

Degree of necrosis and degree of inflammation are given scores from 0-18 & the activity is expressed as histological activity index (HAI) e.g. 3/18 or 9/18... etc)

A) Interface hepatitis (piecemeal necrosis)

- Absent..... 0
- Mild (focal in few portal tracts)..... 1
- Mild to Moderate (local in most portal tracts)..... 2
- Moderate (continuous around < 50% of portal tracts)..... 3
- Severe: (continuous around > 50% of portal tracts)..... 4

B) Confluent necrosis

- Absent..... 0
- Focal..... 1
- Zone 3 necrosis in some areas..... 2
- Zone 3 necrosis in most areas..... 3
- Zone 3 necrosis + occasional porto-portal bridging necrosis..... 4
- Zone 3 necrosis + multiple P-C bridging necrosis..... 5
- Panacinar or multiacinar necrosis..... 6

C) Focal (spotty) lytic necrosis, apoptosis & focal inflammation

- Absent..... 0
- Maximum one focus per 10x objective..... 1
- One to four foci per 10x objective..... 2
- Five to ten foci per 10x objective..... 3
- More than ten foci per 10x objective..... 4

D) Portal inflammation

- None..... 0
- Mild in some or all portal areas..... 1
- Moderate in some or all portal areas..... 2
- Moderate to marked, all portal areas..... 3
- Marked, all portal areas..... 4

(18/Total)

Ishak Fibrosis Staging System

Stage 0: No fibrosis

Stage 1: Fibrosis of some but not all portal tracts

Stage 2: Fibrosis of most or all portal tracts

Stage 3: Fibrosis of most portal tracts with occasional porto-portal bridging

Stage 4: Fibrosis of most portal tracts with porto-portal and porto-central bridging

Stage 5: Marked bridging fibrosis with occasional nodules (incomplete cirrhosis)

Stage 6: Cirrhosis

METAVIR Activity Scoring System

Piecemeal Necrosis	Lobular Necrosis	Overall Histological activity
0	+	0
0	+	1
0	+	2
1	+	1
1	+	1
1	+	2
2	+	2
2	+	2
2	+	3
3	+	3
3	+	3
3	+	3

Interface hepatitis 0 none 1 mild 2 moderate 3 severe

Lobular necrosis 0 (none or mild) 1 (moderate) 2 (severe)

Histological activity 0 (none) 1 (mild) 2 (moderate) 3 (severe) expressed as A0 A1 A2 & A3

METAVIR Fibrosis Staging System:

Nearly similar to Scheuer's system and is expressed as F0, F1, F2, F3 & F4

Example of METAVIR expression: Chronic interface hepatitis A2F1 means moderate activity & mild fibrosis

Grade Of Activity (Necro-inflammatory Activity):

Grade 0: No necrosis. Minimal inflammation.
Grade 1: No necrosis. Mild inflammation.
Grade 2: Mild necrosis (uniceellular, focal or mild piecemeal necrosis). Mild inflammation
Grade 3: Moderate necrosis (moderate piecemeal or spotty necrosis). Inflammation.
Grade 4: Marked necrosis (marked piecemeal, bridging or multiacinar necrosis). Inflammation.

Stage 0: No fibrosis.
Stage 1: Mild portal fibrosis (confined to portal tracts).
Stage 2: Periportal fibrosis or porto-portal septal fibrosis.
Stage 3: Bridging fibrosis, distorting the architecture, but with no established cirrhosis.
Stage 4: Cirrhosis.

Grade :

- 0: Absent or minimal
- 1: Portal inflammation only.
- 2: Mild or localized interface hepatitis
- 3: Moderate interface hepatitis
- 4: Marked interface hepatitis

- 0: None
- 1: Inflammation without lobular necrosis
- 2: Focal necrosis or apoptosis
- 3: Severe lobular necrosis
- 4: Severe necrosis including bridging or

Stage 0: No fibrosis.
Stage 1: Mild portal fibrosis (confined to portal tracts).
Stage 2: Periportal fibrosis or porto-portal septal fibrosis.
Stage 3: Bridging fibrosis, distorting the architecture, but with no established cirrhosis.
Stage 4: Cirrhosis.

OLD CLASSIFICATION OF CHRONIC HEPATITIS:
Before 1977 chronic hepatitis was classified into persistent, active and lobular types. This classification is no more used:

2-Chronic Active (Aggressive) Hepatitis: It corresponds to the recent scoring system of grade 2 or more activity and any stage of fibrosis. Microscopically: There is necrosis and inflammation. Fibrosis will ultimately develop.

CHRONIC HEPATITIS

Framework disturbed

Fibrosis

Bridging necrosis

piecemeal necrosis

inflammation

DEFINITION A chronic ^①diffuse ^②irreversible ^③liver disease characterized by progressive diffuse necrosis.

Progressive diffuse necrosis of liver cells, associated with framework destruction. Repair by both regeneration (in the form of nodules) and fibrosis, i.e. the normal hepatic architecture and lobular pattern cannot be restored. Restoration of the normal liver functions does not occur since the regeneration nodules have no regular relation to portal tracts, no or eccentric veins and irregular sinusoids. Moreover, hepatocytes in these regeneration nodules are commonly degenerated.

7 GROSS:

- Size:** Commonly reduced (shrunken). May be enlarged (e.g. in cases of biliary cirrhosis).
Consistency is firm due to fibrosis.
Surface & cut section are nodular. According to size of regeneration nodules, cirrhosis is classified into:
 a) **Micro-nodular cirrhosis:** Regeneration nodules are 2-3 mm in diameter.
 b) **Macro-nodular cirrhosis:** (poorer prognosis): Regeneration nodules are more than 3 mm and may reach up to 1-6 cm.
 c) **Mixed micro and macro nodular cirrhosis:**
Colour changes may be distinctive e.g. **yellow** in cases of nutritional or alcoholic cirrhosis, **green** in case of biliary cirrhosis and **dark brown** in case of haemochromatosis.

MICROSCOPY: Loss of normal architecture and replacement by:

- ① • **Regeneration nodules:** These consist of proliferating liver cell plates with an irregular sinusoidal pattern. Central veins are absent or eccentric.
- ② • **Fibrous septa** around the regeneration nodules showing **chronic inflammatory cells** and proliferating bile ducts.

AETIOLOGY AND TYPES:

1- Nutritional and Alcoholic Cirrhosis (Laennec's Cirrhosis)

Pathogenesis: Chronic alcoholism or prolonged severe malnutrition lead to steatosis followed by gradual progressive liver cell loss and cirrhosis.

Gross: shrunken, firm yellowish liver. Micro-nodular type.

Microscopy:

- Regeneration nodules: (see above & describe). The liver cells in these nodules show fatty change. In alcoholic cirrhosis Mallory bodies are also seen.
- Fibrous septa (see above & describe).

2 Post-Hepatitis Cirrhosis: *not post-hepatic*

Pathogenesis: It follows chronic active hepatitis (hepatitis C or B virus)

Gross: Liver is reduced in size, firm & shows a mixed micro-and macronodular pattern.

Microscopy:

- Picture of cirrhosis (regeneration nodules and fibrosis) +
- Picture of chronic active hepatitis (piecemeal necrosis, chronic inflammation ... etc)

3. Post- Necrotic Cirrhosis:

- It is a rare type following diffuse liver necrosis (due to viral hepatitis or toxic hepatitis caused by drugs as isoniazid or chemicals as carbon tetrachloride).
It is a macro-nodular cirrhosis. In many cases the aetiology is unknown (cryptogenic).

↳ most precancerous

Aetiology

Def + gross + Micro + site (diffuse or lived)

Micro + Gross + Intestine
Nodules

* Wh *

* What is $\rightarrow$ Laennec's
* $\rightarrow$ post hepatic
C. Excess

→ Laennec's sign

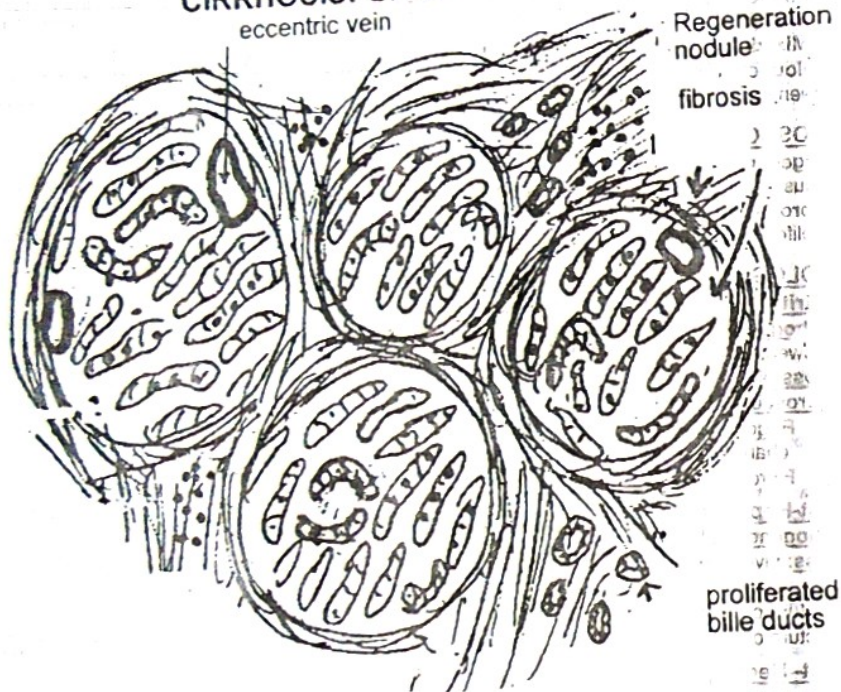


Micronodular cirrhosis

Micronodular cirrhosis

CIRRHOSIS: Gross

eccentric vein



CIRRHOSIS Microscopy

VIP + Comparison

4-Primary biliary cirrhosis (intrahepatic biliary obstruction):

Aetiology: This is an autoimmune disease. In 95% of cases serum anti-mitochondrial antibodies are detected. Other suggested aetiological factors as viral infection & drug hypersensitivity are not much favored.

Sex: The disease mostly affects middle-aged females. Female to male ratio is 9:1.

Gross: Liver is enlarged, green (bile-stained) with micronodular cut surface.

Microscopy: 4 stages: *severe* *solid + proliferation of ducts + scarring + established cirrhosis*

The stage of florid duct lesions: Lymphocytes and plasma cells surround the medium sized ducts associated with focal disruption of the duct basement membranes. Duct epithelial necrosis or degeneration may occur. Some inflammatory cells may infiltrate the duct epithelium through the disrupted basement membrane. Granulomas may develop around the ducts. Finally most of these ducts disappear (ductopenia).

Stage of ductular proliferation: The number of larger bile ducts is diminished due to destruction. This is followed by proliferation of the small ductules. Piecemeal necrosis sometimes occurs, but ductopenia differentiates the condition from cases of chronic hepatitis.

Stage of scarring.

Stage of established cirrhosis: Cirrhosis is due to progressive liver injury caused by bile retention (cholestasis) due to ductopenia. Regeneration nodules are usually micronodular.

5-Secondary Biliary Cirrhosis (extrahepatic biliary obstruction): The differences between secondary biliary cirrhosis and primary biliary cirrhosis are listed in the following table.

	Secondary Biliary Cirrhosis	Primary Biliary Cirrhosis
Aetiology	Obstruction of extra-hepatic bile ducts 1-congenital biliary atresia 2-gall stones 3-cancer head of pancreas. 4-Compression by large lymph nodes Equal female to male ratio.	Autoimmune destruction of intrahepatic bile ducts.
Sex		Female to male ratio is 9:1.
Microscopy:	Extra and intrahepatic bile ducts show bile stasis. The bile ducts may show neutrophils. Prolonged bile stasis leads to progressive liver cell necrosis eventually cirrhosis.	Intrahepatic bile ducts are surrounded by lymphocytes ± granulomas. Basement membrane disruption, bile duct injury & bile duct infiltration by lymphocytes are early features. This is followed by ductopenia, liver cell necrosis & cirrhosis.
Gross:	Liver is enlarged, bile stained and shows micronodular cirrhosis.	Liver is enlarged, bile stained and shows micronodular cirrhosis.
Serum	Elevated cholebilirubin (obstructive jaundice).	1-Elevated cholebilirubin. 2-Autoantibodies.

6-Cirrhosis caused by congenital metabolic disorders:

- Pigment cirrhosis due to haemochromatosis (bronzed diabetes). Micronodular.
- Wilson's disease Macronodular cirrhosis due to excess intestinal absorption of copper.
- Alpha 1 antitrypsin deficiency (micronodular)
- Glycogen storage disease (micronodular) vi) Galactosaemia (micronodular)

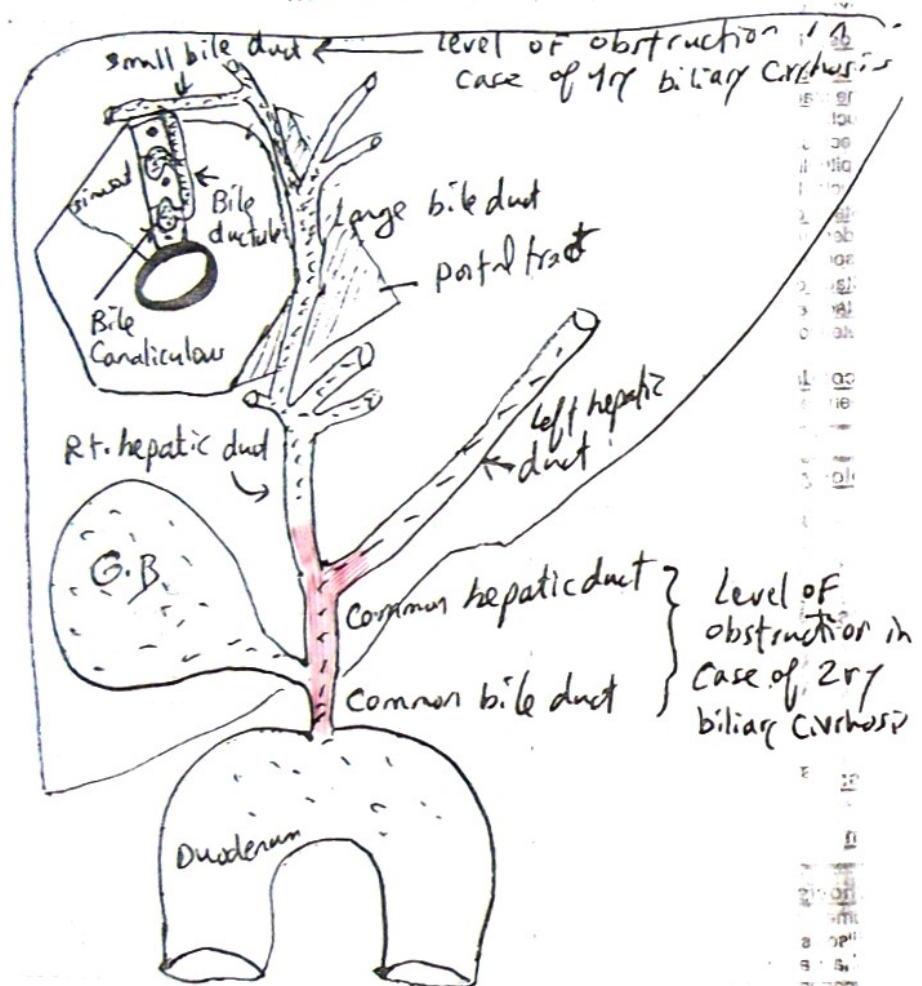
7-Cirrhosis related to circulatory disorders: (CVC Liver) not in heart but in liver due to RT

- Cirrhosis due to chronic venous congestion of the liver (cardiac cirrhosis) is extremely rare.
- Cirrhosis may rarely develop in cases of veno-occlusive disease or Budd-Chiari syndrome.

8-Other rare types of cirrhosis:

- Syphilitic cirrhosis
- Cirrhosis associated with ulcerative colitis.
- Cirrhosis complicating diabetes mellitus.
- Indian Childhood Cirrhosis: Occurs in Indian children. Unknown aetiology.
- Cryptogenic Cirrhosis: This is cirrhosis of undetermined cause

level of obstruction in
case of 1st biliary obstruction



Level of obstruction in case of 2ry biliary cirrhosis

*VIP $\rightarrow$ lipid *

of the circulation +
Circulation lipid +
as complications

Mechanism:

- Compression of the portal vessels by regeneration nodules and fibrosis
 - Development of anastomosis between portal veins and hepatic arteries
- Effects:**

Effects:

- Splenomegaly followed by ^{↑ function} hypersplenism which leads to pancytopenia.
- Varicosities: Oesophageal varices, piles, caput medusae...
- Ascites (see below for the mechanism, describe).
- Congestion of stomach and intestine.

2 hyper $\leftrightarrow$ hyperproteinuria per tal
1 hypo $\rightarrow$ hypoproteinemia

- Hypoproteinemia (due to liver dysfunction) → lowered osmotic pressure
- Hyperaldosteronism (due to liver dysfunction) → salt & water retention

• لَوْ عَرَفْتُمْ

Mechanism: Impaired liver functions in case of cirrhosis is due to continuous loss of liver cells & disturbance of hepatic circulation.

Effects & Manifestations

- Jaundice (hepatocellular type).
- Hypoproteinaemia due to decreased formation of plasma proteins.
- Vitamin deficiency (Vitamin K, A, B12, Folic acid...).
- Coagulation defects due to deficiency of fibrinogen, prothrombin and factors V, VII, IX & X.
- Anaemia due to repeated hemorrhages (from oesophageal varices and piles), hypersplenism (due to splenomegaly) and B12 and folic acid deficiency.
- Hypoglycaemia : due to defects in carbohydrate metabolism.

B. Phalung 30 کر
 Liver
 P. 156

1975

- **Hormone disturbances**; Due to decreased inactivation of hormones in liver.
 - 1- **Elevation of serum aldosterone** → salt and water retention.
 - 2- **Elevation of serum oestrogen** → This leads to:
 - **Palmar erythema** → due to V.D.
 - **Arterial spider** (spider-like arterial dilatation on face, neck)
 - In males: **Gynecomastia**, testicular atrophy & loss of lipid, loss of axillary & pubic hair.
 - In females: **Menstrual disturbances**.
- **Ascites** due to portal hypertension, hypoproteinaemia and salt and water retention.

15/5

h and factors V, VII, IX & X.

(scars and piles),

efficiency.

ones in liver.

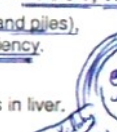
Loss of ability to produce bile

gynaecomastia

axillary & pubic hair.

water retention.

neurological disturbances



- **Hepatic (ammonia) encephalopathy & hepatic coma:** These are neurological disturbances

(apathy, disorientation, tremors and finally coma) caused by toxic amines. These amines are normally formed in intestine & detoxified in liver. Due to liver failure they pass to systemic circulation & act on brain.

- Foetor hepatis: This is a peculiar sweetish smell at the mouth due to presence of methy

mercaptan derived from unmetabolized methionin.

- Renal failure (hepatorenal failure). Mechanism is not fully understood.

Aetiology of Liver Failure: Liver failure is due to severe liver damage as in cases of:

- Cirrhosis
 - Chronic biliary obstruction (biliary cirrhosis)
 - Primary & metastatic liver tumors
 - Granulomas as tuberculosis & sarcoidosis
- b) Acute liver failure due to massive necrosis (fulminant hepatitis)

Hepatocellular Carcinoma:

5-Pancytopenia (due to hypersplenism) may be also prominent.

5-Fancytopent

0 + F

Cirrhosis Complications

- ② Ascites
③ Hepatocellular failure
④ Hepatocellular carcinoma
⑤ Pancreatopenia

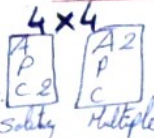
White Knight one

VIP

LIVER ABSCESS

SOLITARY ABSCESS

- 1-Amoebic abscess.
- 2-Infected hydatid cyst.
- 3-Following penetrating injury.
- 4-Complicating cholecystitis.



MULTIPLE ABSCESSES

- 1-Amoebic abscess may be multiple.
- 2-Pyæmic abscesses.
- 3-Actinomycotic abscesses.
- 4-Complicating cholangitis.

TUMORS OF THE LIVER

BENIGN TUMORS

- 1-Cavernous Hemangioma:
- 2-Liver Cell Adenoma: Rare. Affects females using oral contraceptives & athletes taking anabolic steroids.
- 3-Bile Duct Adenoma (or Cystadenoma): Rare.

MALIGNANT TUMORS

HEPATOCELLULAR CARCINOMA (HEPATOMA)

Most common 1st liver malignancy.

Predisposing factors:

- Cirrhosis; particularly macronodular.
- Chronic hepatitis B or C.
- Aflatoxins: derived from *Aspergillus flavus* fungus contaminating "moldy" grains and peanuts.

Gross: 3 patterns:

- A large solitary tumor.
- Multicentric (multinodular) pattern: Multiple tumor nodules.
- Diffuse: The whole liver is almost entirely infiltrated by the tumor.

Microscopy:

- The classic hepatocellular carcinoma consists of pleomorphic polyhedral malignant hepatocytes arranged in a trabecular or acinar patterns, separated by little vascular stroma.
- The rare fibrolamellar carcinoma is a special variant composed of columns of large eosinophilic hepatocytes with very well differentiated features, separated by parallel (lamellar) bundles of collagen. This neoplasm tends to occur in younger individuals & has much better prognosis than the classic type.

Spread:

- Direct within the liver.
- Lymphatic to hilar lymph nodes.
- Through the hepatic veins to lungs then other organs.
- Through portal veins leading to metastases in liver itself.

CHOLANGIOCARCINOMA (CHOLANGIOMA and BILE DUCT CARCINOMA)

Gross: Single or multiple tumor masses.

Microscopy: Adenocarcinoma, showing mucin secretion. Marked sclerosis is common.

Spread: Relatively slower than hepatocellular carcinoma. Same routes of spread.

HEPATOBLASTOMA: A rare malignant embryonic tumor occurring in infants. Rapidly fatal.

Gross: It appears as a large mass with extensive necrosis and hemorrhage.

Microscopy: Malignant immature hepatocytes & mixed mesenchymal elements (bone, cartilage, fibrous tissue).

embryonic rapidly fatal
single pattern
mixed mesenchymal elements in Microscopy



ANGIOSARCOMA: A highly malignant vascular neoplasm.

METASTATIC (SECONDARY) TUMORS: Common tumors

Routes of spread to liver:

- a) Via portal vein from cancer stomach and intestine.
- b) Via hepatic artery from cancer lung whether 1st or 2nd (e.g. from breast).
- c) Via lymphatic spread from cancer lung or breast.
- d) Direct spread from cancer stomach, gall bladder, colon...

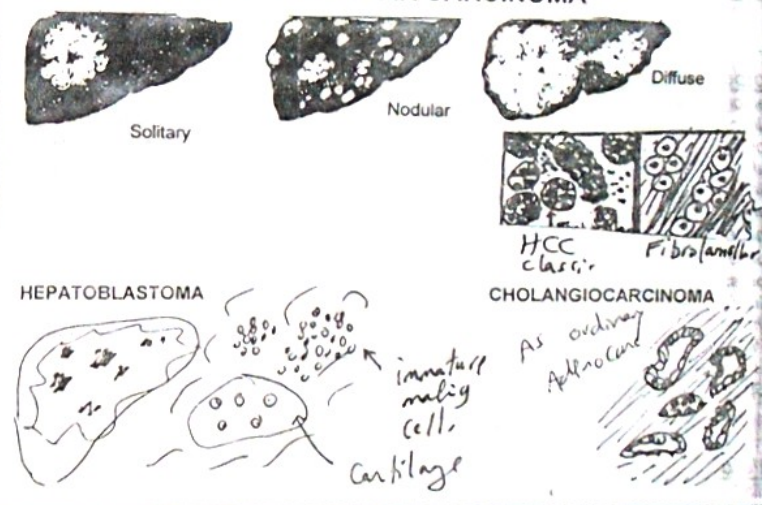
Gross: The liver is enlarged and shows multiple circumscribed metastatic nodules. The large ones may show central necrosis (umbilication).

Microscopy: Resembles the primary.

CLINICAL EFFECTS OF MALIGNANT LIVER TUMORS:

- Hepatomegaly.
- Jaundice
- Portal vein thrombosis
- Ascites.
- Liver failure.
- Elevation of serum alpha fetoprotein in cases of hepatocellular carcinoma & hepatoblastoma.

HEPATOCELLULAR CARCINOMA



CAUSES OF HEPATOMEGALY (Liver Enlargement)

- 1-Inflammatory diseases (viral hepatitis, liver abscesses, malaria, granulomas...etc)
- 2-Degenerative diseases (mainly steatosis e.g. in alcoholics, diabetics, obese...)
- 3-Metabolic disorders as glycogen storage disease, hemochromatosis...etc.
- 4-Blood diseases as leukemia
- 5-Neoplastic disease (Benign tumors, primary malignant tumors, metastases...enumerate).
- 6-Some types of cirrhosis (as biliary cirrhosis)
- 7-Amyloidosis
- 8-Vascular disorders as Nutmeg liver, Budd Chiari and veno-occlusive diseases.

* 9-Traumatic Hematoma
→ not tumor?
→ can be it

Cirrhosis
doesn't cause
enlargement

Metastatic
carcinoma

JAUNDICE (X)

DEFINITION: The normal amount of bilirubin in blood is less than 1 mg/100 ml. Levels of bilirubin above 2 mg/100 ml lead to clinical jaundice, defined as yellow coloration of all tissues except CNS due to hyperbilirubinaemia (haemobilirubin and/or cholebilirubin depending on the type of jaundice).

BILE METABOLISM & MECHANISM OF FORMATION OF BILE PIGMENTS:

- **Hemobilirubin:** Bilirubin is formed in the reticuloendothelial system from broken erythrocytes. It then passes to blood where it combines with albumin forming haemobilirubin. It cannot pass in urine as it is insoluble in water. It can be detected by the Van den Bergh reaction which is indirect in this case i.e. no colour is produced with the diazo reagent, but when alcohol is added it unmasks bilirubin from albumin and the reaction now occurs between bilirubin & diazo reagent.
- **Cholebilirubin:** In the liver haemobilirubin leaves albumin and becomes conjugated with glucuronic acid forming cholebilirubin, which passes with bile and becomes reduced in the intestine into sterkobilinogen (giving brown coloration to stools). Some sterkobilinogen is absorbed into the blood where it becomes excreted in urine (urobilinogen). cholebilirubin is water-soluble & is excreted in urine. It can be detected by Van den Bergh reaction which is direct, needing no alcohol to be completed.

TYPES OF JAUNDICE:

HAEMOLYTIC JAUNDICE

Aetiology: Excessive hemolysis of erythrocytes occurs in cases of:

- 1-Haemolytic anaemias.
- 2-Rh incompatibility (erythroblastosis foetalis).
- 3-Incomplete blood transfusion.
- 4-Snake bite.
- 5-Malaria.
- 6-Internal hemorrhage.

Pathological Features:

- 1-Blood: Increased haemobilirubin (indirect Van den Bergh reaction).
- 2-Stools: Excess sterkobilinogen (dark stools).
- 3-Urine: No bilirubin (acholuric). Excess urobilinogen.
- 4-Others:

- a) Pigment stones in gall bladder due to excess bilirubin in bile.
- b) Haemosiderosis.
- c) Splenomegaly due to reticuloendothelial hyperplasia.

OBSTRUCTIVE JAUNDICE

Aetiology: Obstruction of bile ducts may be due to:

- 1-Biliary Stones.
- 2-Congenital atresia.
- 3-Compression by enlarged lymph node.
- 4-Malignant infiltration as in cancer head of pancreas or cancer ampulla of Vater.

Pathological features:

1-Blood:

- a) Increased cholebilirubin (direct Van den Bergh reaction).
- b) Increased bile salts (lead to severe itching).
- c) Increased cholesterol leading to xanthomata (yellow skin patches).
- d) Increased alkaline phosphatase.
- e) Hypoprothrombinaemia due to vitamin K deficiency caused by reduced intestinal absorption of this fat soluble vitamin due to absence of bile.

2-Stools:

- a) Steatorrhea due to presence of excessive unabsorbed fat. The stools appear bulky and greasy.
 - b) Clay coloured due to absence of sterkobilinogen.
- 3-Urine is dark as it contains cholebilirubin.
- 4-Others: a) Bile stasis favors infection producing cholangitis & multiple liver abscesses.
b) Secondary biliary cirrhosis occurs in prolonged cases.

HEPATOCELLULAR JAUNDICE (HEPATIC JAUNDICE)

Aetiology: Severe liver cell damage as in cases of:

- 1-Acute or chronic hepatitis.
- 2-Cirrhosis.
- 3-Malignant tumors.

Pathological features:

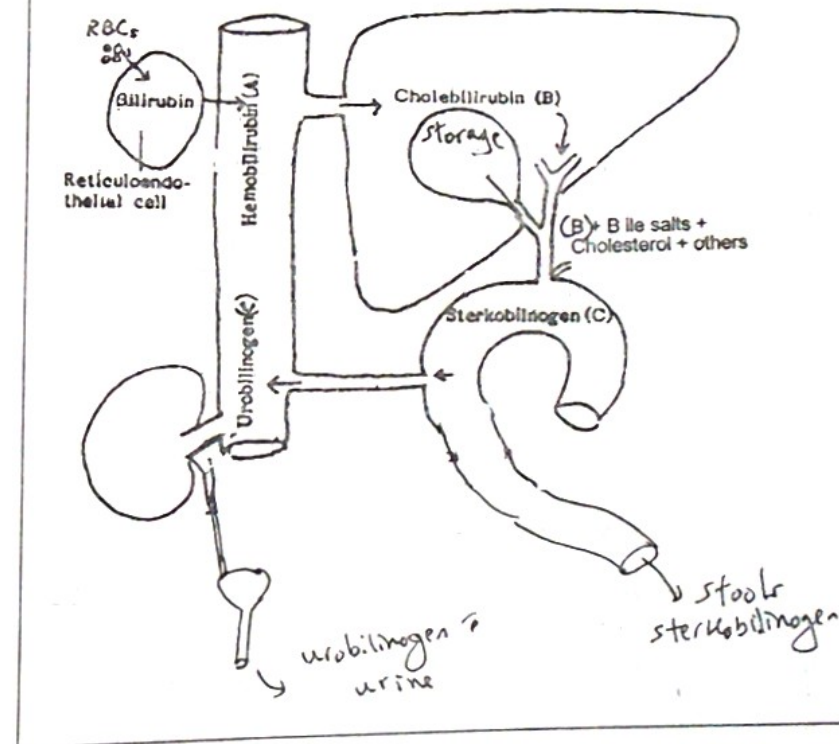
1-Blood contains higher levels of both haemobilirubin and cholebilirubin (biphasic Van den Bergh reaction). Although conversion of both haemobilirubin into cholebilirubin by the diseased liver is reduced; some of the later regurgitates in the blood because liver disease is associated with some intra- hepatic biliary obstruction.

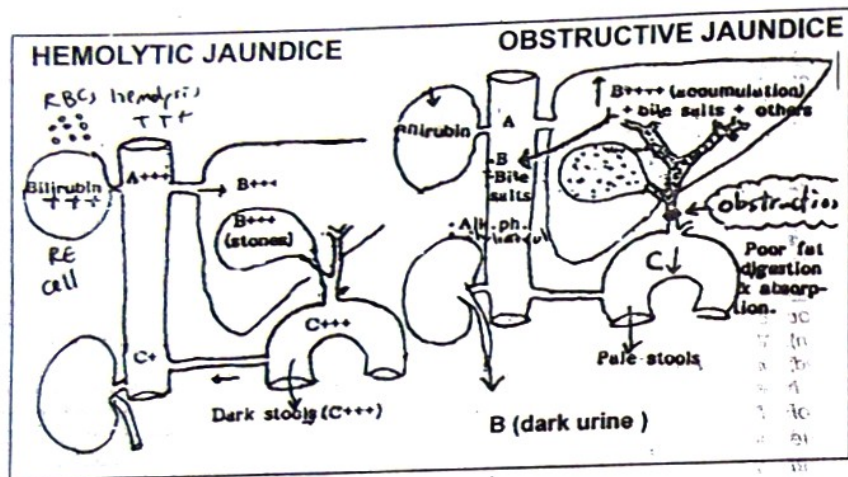
2-Stools: Paler than normal.

3-Urine contains some cholebilirubin.

4-Others: Abnormal liver function tests.

FORMATION OF BILE





VENO-OCCLUSIVE DISEASE & BUDD-CHIARI SYNDROME

1-Veno-occlusive disease of the liver. It mainly occurs in Tropical countries due to ingestion of alkaloids present in plants used in herbal medicine → progressive subintimal fibrosis → occlusion of hepatic veins → marked sinusoidal congestion → hemorrhage & liver cell necrosis → acute liver failure. Survivors develop cirrhosis.

2-Budd-Chiari Syndrome: This is thrombotic occlusion of the major hepatic veins (idiopathic or due caused by malignant invasion) → marked sinusoidal congestion → hemorrhage & liver cell necrosis → liver failure & rarely cirrhosis.

STEATOHEPATITIS

This hepatic steatosis, accompanied by inflammation, progressing to fibrosis or cirrhosis. It may be:

1-Alcoholic steatohepatitis (ASH): characterized by one or more of the following:

a) Fatty liver (steatosis) b) Alcoholic hepatitis: c) Alcoholic cirrhosis.

2-Non-alcoholic steatohepatitis (NASH).

GRANULOMATOUS HEPATITIS

Hepatic granulomas may occur in many conditions as:

1-bilharziasis 2-tuberculosis 3- sarcoidosis 4- primary biliary cirrhosis. 5-others.

PRIMARY SCLEROSING CHOLANGITIS

A disease of unknown aetiology: (? autoimmune). May occur in association with ulcerative colitis, (up to 70%). It is characterized by portal inflammation & progressive "onion-skin" type periductal fibrosis affecting the medium-sized or larger intrahepatic bile ducts → complete duct obliteration → marked cholestasis

PEDIATRIC LIVER DISEASES

1-NEONATAL HEPATITIS: May be idiopathic, metabolic (as α -1 antitrypsin deficiency or galactosemia), post-viral (CMV) or bacterial (*Treponema pallidum*). Idiopathic and viral types are usually self limited, but other types may lead to cirrhosis.

2-EXTRAHEPATIC AND INTRAHEPATIC CHOLESTASIS e.g. extrahepatic biliary atresia.

3-REYE'S SYNDROME: Rare. May follow viral illness. Characterized by fatty liver, encephalopathy & may be fatal.

4-METABOLIC AND STORAGE DISEASES.

5-CONGENITAL HEPATIC FIBROSIS AND POLYCYSTIC DISEASE.

6-CHRONIC HEPATITIS (viral or non-viral types).

7-TUMORS: Benign as mesenchymal hamartoma, infantile hemangioendothelioma & malignant as hepatoblastoma.

Appendicitis III = surgical bec small narrow lumen just perforate
Bladder acute cholecystitis → III by medical bec. wide large lumen rarely perforate
Chapter VII

DISEASES OF THE GALL BLADDER, PANCREAS & PERITONEUM

DISEASES OF GALL BLADDER

ACUTE CHOLECYSTITIS

Def: acute inflammation of mucosa of gall bladder

AETIOLOGY:

- 1-Chemical irritation by concentrated bile occurs when a stone is impacted in the cystic duct.
- 2-Bacterial infection (*Streptococci*, *E. coli*, typhoid bacilli...) by direct lymphatic or blood spread.
- 3-Irritation by pancreatic enzymes in case of pancreatic reflux.

PATHOLOGICAL FEATURES:

Inflammation may be catarrhal or suppurative:

- 1-Swollen oedematous hyperaemic wall. The serosal covering is opaque
- 2-Ulcerated mucosa
- 3-Turbid bile, which may be mixed with pus and blood.

4-Empyema of gall bladder (distension with pus) occurs in severe cases if cystic duct is obstructed. Perforation or local spread of infection may lead to pericholecystic liver abscess. Obstruction of vessels due to gall bladder distention may lead to gangrene, where the gall bladder appears black and friable.

Microscopy: Mucosal shedding, dilated capillaries, neutrophils, pus cells...

COMPLICATIONS:

- 1-Empyema.
- 2-Gangrene
- 3-Perforation → pericholecystic abscess and/or septic peritonitis
- 4-Chronic cholecystitis.

CHRONIC CHOLECYSTITIS

AETIOLOGY:

- 1-May follow acute cholecystitis.
- 2-May start chronic due to prolonged irritation by gall stones (chronic calculous cholecystitis).

PATHOLOGICAL FEATURES

- 1-Thick fibrotic wall with adhesions.
- 2-If cystic duct is obstructed → distension of gall bladder with clear bile (hydrops) or mucus (mucocoele).
- 3-If cystic duct is patent, the fibrotic gall bladder becomes contracted.
- 4-Gall stones are very common (as a cause or as a result of chronic cholecystitis).

Microscopy:

- 1-The wall shows chronic inflammatory cells and fibrosis.
- 2-Mucosa may be hyperplastic. Hyperplastic mucosa may extend deep towards submucosa and musculosa (cholecystitis glandularis proliferans). Squamous metaplasia may also occur.

COMPLICATIONS:

- 1-Acute attacks (acute cholecystitis).
- 2-Formation of gall stones.

GALL STONES (CHOLELITHIASIS)

Development of biliary stones is commonest in the gall bladder (gall stones). More common in females particularly fatty fertile females around the age of forty.

Handwritten notes in Arabic and English discussing complications like fibrosis, stones, and no spread, and the condition cholelithiasis.

AETIOLOGY:

- 1. Abnormal composition of bile:**
 - a) Excess cholesterol due to hypercholesterolemia (e.g. obesity) → Cholesterol stones.
 - b) Excess bilirubin in cases of hemolytic jaundice → pigment stones.
 - c) Decreased concentration of bile salts (loss of emulsification) → mixed stones.
- 2. Stasis of bile:** e.g. due to pregnancy or obstruction of cystic duct. Stasis leads to a concentration of bile due to absorption of water.

Infection (cholecystitis): leads to formation of mixed stones due to:

- Decrease of bile salts (loss of the emulsifying action).
- Formation of a nucleus (bacteria, fibrin, cells...) around which bile constituents become precipitated.

TYPES OF GALL STONES:

1-Pure Stones (Metabolic Stones): 10%

- Cholesterol Stone:** Usually solitary, yellow, 1-5 cm in diameter. It has a mammillated surface (mulberry-like). Cut surface shows radiations.
- Pigment Stones:** Multiple dark small stones with smooth surfaces. Consist of calcium bilirubinate.
- Calcium carbonate stones:** Single or multiple, chalky white with smooth surfaces. Very rare.

2-Mixed Stones: 80%: Common in association with chronic cholecystitis (infective stones) due to formation of a nucleus (bacteria, inflammatory cells, shed epithelial cells, fibrin) and due to decreased bile salt concentration. They are multiple, 1-1.5 cm in diameter with faceted surfaces. Cut section shows a central nucleus surrounded by concentric laminae of cholesterol (yellow) bile pigments (dark) and calcium carbonate (white).

3-Combined Stones: 10%: If a cholesterol stone exists in infected gall bladder it may act as a nucleus around which other bile constituents may precipitate.

EFFECTS AND COMPLICATIONS:

1-Migration of stones: This leads to biliary colic and biliary obstruction.

2-Obstruction:

- Cystic duct obstruction leads to acute cholecystitis, empyema, mucocoele...
- Common bile duct obstruction → obstructive jaundice, ascending cholangitis & secondary biliary cirrhosis.
- Obstruction of ampulla of Vater may lead to acute hemorrhagic pancreatitis.
- Intestinal obstruction (gall stone ileus) may occur if an inflamed gall bladder gets adherent to a loop of intestine accompanied by fistula formation through which a big gall stone may pass causing intestinal obstruction.

3-Infection: → cholangitis and cholecystitis.

4-Squamous metaplasia and malignancy.

CHOLESTEROLOSIS OF GALL BLADDER

This is considerable deposition of cholesterol in the mucosa of the gall bladder with or without an accompanying cholesterol stone formation. The mucosa appears yellowish and mammillated (strawberry-like). Microscopically there are foam histiocytes and chronic inflammation.

TUMORS OF THE GALL BLADDER

Benign tumors as adenomatous polyps, fibroma, fibroadenoma, leiomyoma, angioma, Lipoma & **Malignant tumors** as carcinoma, sarcoma, carcinoid & lymphomas.

Carcinoma of the Gall Bladder: More common in females & predisposed to by gall stones. Grossly the bladder is infiltrated by a malignant firm growth.

Microscopically usually adenocarcinoma.

Spread: a) direct to liver b) lymphatic to regional nodes c) blood d) transcoelomic.

Adeno Carcinoma of gall bladder more common in ♀

Gross

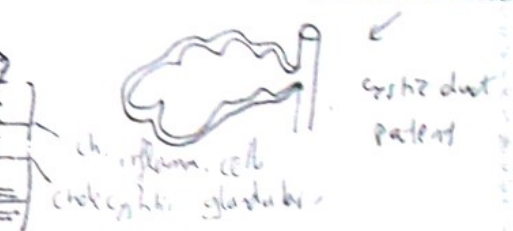
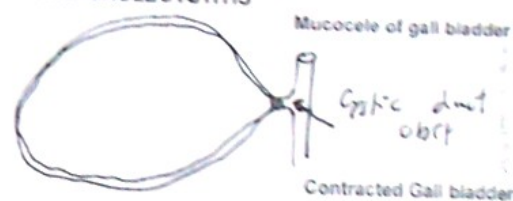
CHRONIC CHOLECYSTITIS



Microscopy

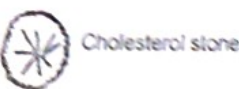


Types of gall stones

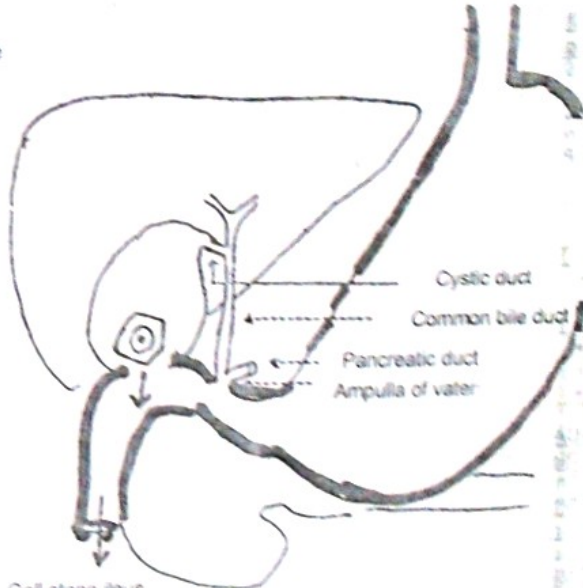


GALL STONES

Sites of stone obstruction



Pigment stones



Gall stone ileus

Handwritten notes in Arabic script at the bottom of the page.

DISEASES OF THE PANCREAS

ACUTE HAEMORRHAGIC PANCREATITIS

It is a clinical syndrome of important medical emergency, resulting from the escape of activated pancreatic digestive enzymes from the duct system into the pancreatic parenchyma, leading to extensive destruction of pancreatic and peri-pancreatic tissue and acute inflammation.

Aetiology & Pathogenesis: Pancreatic necrosis, hemorrhage and inflammation may be due to:

- 1-Obstruction of ampulla of Vater by gall stone. Thus bile passes into pancreatic duct and activates trypsinogen into trypsin which digests the pancreatic tissue.
- 2-Excess alcohol abuse may → increased secretion of pancreatic juice → rupture of pancreatic ducts.
- 3-Accidental surgical injury of pancreas
- 4-Hyperparathyroidism → $\uparrow \text{Ca}^{2+}$ → $\uparrow$ stone in gallbladder
- 5-Polyarteritis nodosa
- 6-Viral and bacterial infections

Pathological Features:

- 1-Swollen pancreas with patches of necrosis and hemorrhage.
- 2-Secondary infection may occur leading to suppuration (pus formation).
- 3-Fat necrosis due to action of pancreatic lipase on peritoneal fat cells → glycerol & fatty acids, the later combine with calcium → patches of calcium soap (see general pathology)
- 4-Chemical peritonitis. The peritoneal cavity may contain a brownish serous fluid (pancreatic ascites). The fluid contains altered blood, fat globules and high level of amylase.
- 5-Rise of serum amylase and lipase as they reach blood from the necrotic areas.

Clinical Picture: Acute abdomen.

Complications:

- 1-Shock and death.
- 2-Gangrene (rare) leading to severe toxemia and death.
- 3-Chronic pancreatitis. It follows mild attacks of acute peritonitis. The pancreas is firm and nodular due to fibrosis. The effects include steatorrhea and diabetes mellitus.
- 4-Pancreatic pseudocyst: A cyst with fibrous wall and bloody contents with no epithelial lining.

TUMORS OF THE PANCREAS

1-Tumors Of The Exocrine Part:

- Benign: cystadenoma
- Malignant: Adenocarcinoma

2-Tumors Of The Endocrine Part: (Islet Cell Tumors)

- Gastrinoma: Secretes gastrin.
- Insulinoma: Secretes insulin.
- Glucagonoma: Secretes glucagon.

CARCINOMA OF PANCREAS:

Risk factors: 1-Diabetes mellitus particularly in females. 2-Dietary factors: as high fat diets. 3-Chronic pancreatitis 4-Cigarette smoking.

Sites: 1-Head of pancreas (commonest). 2-Body and Tail (less common).

Gross: An infiltrative irregular hard grayish mass affecting head, body or tail of pancreas.

Microscopy: About 99% arise from the ducts (duct carcinoma) and 1% from acini. It is commonly well differentiated adenocarcinoma with marked fibrosis and perineural invasion. Other types include adenosquamous carcinoma and anaplastic carcinoma.

→ Primary malignant neoplasm arising from pancreas
 Aetiology = unknown but predisposing factors: age > 40 sex ♀
 + Risk factors: cigarette

(A)+VIP+ GSP
 → Case



rare if Patient didn't die

endocrine
exocrine

pancreas
prostate
bone

من السرطان = Pancreatic

40 factors

chronic pancreatitis

Spread:

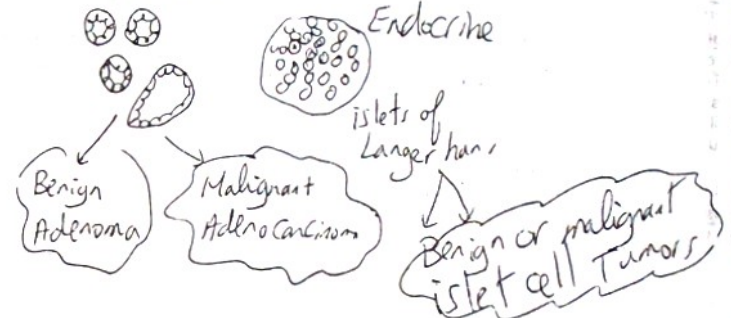
1-Direct:

- a) From carcinoma of head to common bile duct causing obstructive jaundice. Spread to duodenum leads to duodenal obstruction.
 - b) From carcinoma of body and tail to spleen, kidney and vertebra. No jaundice occurs.
- 2-Lymphatic to regional lymph nodes
- 3-Blood to liver, lungs, etc. = LBLB → take care lungs before liver bec. not portal
- 4-Transcoelomic spread associated with hemorrhagic ascites.

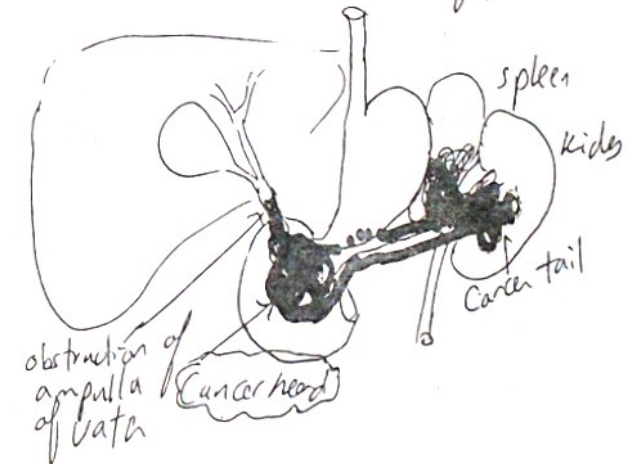
Complication
 1. hemorrhage
 2. infection
 3. distal metastasis
 4. loss of function
 5. steatorrhea
 6. Diabetes Mellitus

Exocrine
Acini & ducts

PANCREATIC TUMORS



Adenocarcinoma of pancreas



obstruction of ampulla of Vater
 * انحصار مادة السرطان في الكبد
 Read
 obstruction of pancreas
 من السرطان في الكبد
 من السرطان في الكبد

DISEASES OF THE PERITONEUM

SUPPURATIVE (SEPTIC) PERITONITIS

→ Def. acute suppurative inflammation of peritoneum

Aetiology: Pyogenic bacteria (E. coli, staphylococci, streptococci). They reach the peritoneum by:

- 1-Direct spread from appendicitis, cholecystitis, diverticulitis, salpingitis.
- 2-Perforation of ulcers (peptic, tuberculous, typhoid, amoebic).
- 3-Penetrating abdominal wounds.
- 4-Complications of abdominal operations due to injury of gut or defective sterilization.

CO
NOT

Pathology: The affected peritoneum is swollen, congested and shows inflammatory exudate. There are two types of affection:

1-Localized Peritonitis: Around the source of infection inflammation may be localized by the greater omentum (policeman of the abdomen) and fibrin. The intestinal loops become adherent by fibrin. The resulting inflammatory mass may resolve or suppurate resulting in a peritoneal abscess. Fate of this peritoneal abscess includes:

- a) Resolution.
- b) Rupture
 - i) into peritoneal cavity leading to diffuse peritonitis.
 - ii) into abdominal wall (sinus) or into loops of intestine (fistulae).
- c) Healing leads to peritoneal adhesions which may cause intestinal obstruction.

2-Diffuse Peritonitis: The peritoneal cavity contains excess pus. Almost fatal from severe toxæmia or from paralytic ileus.

OTHER TYPES OF PERITONITIS

- 1-Tuberculous peritonitis (see general).
- 2-Rheumatic peritonitis (see rheumatic fever).
- 3-Chemical (sterile) peritonitis due to irritation by blood as in cases of ruptured intra-abdominal aneurysm, bile as in rupture of gall bladder or pancreatic enzymes as in acute hemorrhagic pancreatitis.

ASCITES

(A) VIP

This is accumulation of fluids (transudate, exudate or lymph) in peritoneal cavity.

1-Transudative Ascites: It is caused by:

- Generalized oedema (cardiac, nutritional or renal).
- Portal hypertension and liver failure.
- Constrictive pericarditis.
- Pedunculated ovarian tumors when their pedicles are twisted.
- Meig's syndrome.

2-Exudative Ascites:

Due to peritonitis and peritoneal metastases (hemorrhagic ascites).

3-Chylous Ascites: Due to lymphatic obstruction as in filariasis.

① Define Ascites
② enumerate Types
③ Mention Mechanism of Ascites in portal hypertension?
Liver cirrhosis induces Ascites by
① portal hypertension
② hypoalbuminemia
③ salt & water retention

TUMORS OF PERITONEUM

Benign tumors are rare

Malignant tumors :

- 1) Mesothelioma (rare)
- 2) Retroperitoneal sarcomas
- 3) Metastases: common in cases of cancer stomach, colon, pancreas, liver, ovary (& can occur with other malignancies). It can be due to transcoelomic spread or other routes as blood spread. Hemorrhagic ascites accompanies peritoneal metastases. Metastatic tumors from mucoid carcinoma may cause multiple peritoneal mucinous masses leading to pseudomyxoma peritonii which is better called peritoneal mucinous carcinomatosis

Acute diffuse Proliferative G.N. "Post streptococcal G.N." <i>VIP</i>	Rapidly progressive G.N. "Crescentic G.N." <i>VIP</i>	Minimal change G.N. "Lipoid Nephrosis" <i>VIP</i>	Membrano proliferative G.N. "Mesangiocapillary G.N." <i>Tram track</i> <i>Capillary Basement membrane</i>	Membranous G. N.	Focal Proliferative G.N.	Focal Segmental glomerulosclerosis	Diffuse Mesangial Proliferative G.N.
- Immune complex disease affecting children & young adults. - Starts as upper R.T inf. With nephrogenic strains of group A beta hemolytic streptococci. 1-4 weeks => immune complex are deposited on BM of glom. capillaries => destruction BY: lytic effect of complement - proteolytic enzymes by attracted neutrophils + diffuse proliferation	- a-) follow acute diffuse G.N. - b-) IDIOPATHIC - c-) Part of GOODPASTURE'S syndrome rapidly progressive G.N. + Pulmonary hemorrhages - d-) secondary to "SLE OR Henoch-Shonlein purpura."	- More in children - Unknown aetiology - Immune mechanism is suspected? Bec. - a-) many cases follow resp. infection. - b-) respond well to corticosteroids ttt.	- Children or adults - Unsettled aetiology - May be post infection	- Adults are affected: - a-) 85% idiopathic. - b-) secondary to : 1-) SLE 2-) Carcinoma 3-) Diabetes. 4-) some drugs mercury gold & penicillamine 5-) Infections malaria, HBV, S. mansoni	- a-) Idiopathic. - b-) secondary to : SLE, Goodpasture syndrome, Henoch-Shonlein purpura, Subacute inf. endocarditis - Some cases may follow upper resp. infections	- Affecting children MORE - a-) Idiopathic - b-) secondary to "HEROIN ABUSE".	- a-) Idiopathic - b-) Henoch-Shonlein purpura - c-) SLE - d-) IgA nephropathy "BERGER'S disease."
Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages. <i>check + eye</i>	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.	Unremarkable changes. <i>OK, IP</i>	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.	Mild bilateral kidney enlargement. Cortical edema & petechial hemorrhages.
- a-) Glomeruli are enlarged: - proliferation of epithelial, endothelial and mesangial cells. - Neutrophils in glomerular capillaries. - Bowman's capsular space: Neutrophils, R.B.C's & albumin. - b-) Tubules: cloudy swelling & casts "mainly blood casts" - c-) Interstitium: oedema & neutrophils - d-) EM & Immuno fluorescence: "Humpy-Lumpy" sub epithelial immune complex deposit "IgG, IgM & Complement"	- a-) Glomeruli are enlarged: - focal necrosis & capillary thrombosis. - Prolif. Of mesangial cells. - Crescents' prolif. Monocytes, fibrin & parietal epithelial cells. - b-) Tubules: cloudy swelling & casts - c-) Interstitium: inflammation. - d-) EM & Immuno fluorescence Linear sub endothelial immune complex deposit "IgG"	- a-) LM: unremarkable changes. "glomeruli" - b-) lining cells of PCT: LIPIDS "from reabsorbed lipopn." - c-) E.M & I. Fluorescence: - Diffuse effacement of foot processes of visceral epithelial cells. - No Immunoglobulin deposits.	- Enlarged glomeruli: - a-) mesangial cells & matrix: Proliferation. - b-) Capillary BM: thick => "double contoured OR tram-track" + Wire Loop - c-) E.M & I. Fluorescence - Type I: sub endothelial immune complex deposit "IgG, M & complement." - Type II: Dense complement deposition in GBM "Dense deposit disease OR Alternate pathway disease."	- a-) GBM: thickened, exhibit hair comb appearance of outer part of membrane due to Igs deposition - b-) EM & Immuno fluorescence: sub epithelial deposits of IgG.	- a-) Some glomeruli shows BM thickening and mesangial cells proliferation. - b-) EM & Immuno fluorescence: IgM deposition.	- a-) Focal Hyalinosis and sclerosis of juxtaglomerular glomeruli. - b-) EM & Immuno fluorescence: Mesangial deposits of IgM & Complement.	- a-) Glomeruli shows + Mesangial cells & matrix. - b-) EM: mesangial dense deposits. - c-) I. Fluorescence mesangial deposits of IgG & C3. In BERGER'S disease: IgA and C3 are detected
- a-) Fever & RIGORS - b-) Nephritic syndrome - c-) HTN. - d-) Urine: oliguria, hematuria "urine: coca cola like", mild proteinuria, high specific gravity "1035" & CASTS - e-) Blood: ↑ Urea & creatinine, mild anemia.	Nephritic OR Nephrotic syndrome.	Nephrotic syndrome <i>Commonest cause of nephrotic in children</i>	Nephrotic OR Nephritic syndrome OR combined. <i>MCQ</i>	Nephrotic Syndrome <i>Commonest cause of nephrotic in adults</i> <i>MCQ</i>	Nephrotic Syndrome <i>MCQ</i>	Nephrotic Syndrome <i>MCQ</i>	Nephrotic Syndrome Hematuria may be prominent. <i>MCQ</i>
- a-) Recovery in more than 95% of children and in 2/3 of adults. - b-) Development of Rapidly Progressive G.N. - c-) Rarely: death from acute RF.	- b-) Rapid progression to acute RF. - c-) Chronic GN "if survive"	Good prognosis... cured by corticosteroid therapy.	Chronic RF develops in 50% of cases of idiopathic MGN within 10 years.	Chronic RF develops in 50% of cases of idiopathic MGN within 2-20 years	1-) May progress to diffuse GN 2-) Chronic RF develops in 50% of cases	Chronic RF develops in 50% of cases	Some cases resolve, others progress to RF.

Points of comparison: Aetiology & Pathogenesis.....Gross.....microscopic.....Clinical picture.....Fate & Course.

• NEPHRITIC Syndrome: - Hematuria, oliguria, mild proteinuria, HTN
- Nephritic edema "starts in lids, particularly in morning then => generalized"

• NEPHROTIC syndrome: Massive proteinuria, hypoproteinemia, hyperlipemia & Generalized edema

• Acute renal failure: Oliguria, rise of blood urea & creatinine.....

• Good pasture's syndrome: rapidly progressive G.N + Pulmonary hemorrhages



→ No Haematuria

White blood cells

	Adult Congenital Polycystic Kidney	Infantile Congenital Polycystic Kidney
Inheritance	Autosomal dominant Inheritance	Autosomal Recessive Inheritance
Site	Both kidneys affected	Both kidneys affected
Aetiology	Failure of communication between convoluted tubules & collecting tubules	Failure of communication between collecting tubules & collecting ducts
1. Degree of enlargement	Marked enlargement of both kidneys	Mild enlargement of Both kidneys
1. Degree of affection	50% of tubules affected	Nearly All tubules affected
lining of cysts	lined by flattened & cuboidal cells	lined by collecting duct cells
Accompanying	Cystic Liver & Cerebral berry aneurysms	Congenital hepatic fibrosis
Death	at adulthood	still birth or during infancy or childhood
Complic.	Chronic renal failure + 25% hypertension + 10% hematuria + 25% infection	Acute renal failure

1. Main cause 2 kidneys
2. Can live with 1/2 kidney
3. Affected = 3x effort to increase pressure

CHAPTER VIII

DISEASES OF THE URINARY SYSTEM

DISEASES OF THE KIDNEY

CONGENITAL ANOMALIES OF THE KIDNEYS

- 1-Agenesis: Absent kidney
- 2-Hypoplasia: Undersized kidney
- 3-Ectopic kidney: Pelvic kidney not ascending to its normal position
- 4-Horse-shoe kidney: Both kidneys are fused at their lower poles.
- 5-Supernumerary kidneys.
- 6-Double ureter or double pelvis.
- 7-Congenital cystic kidneys: VIP (A) + Jar + Case

A Adult Polycystic Disease of the Kidney:

- It may be associated with cystic liver & cerebral berry aneurysms.
- Pathogenesis: Autosomal dominant inheritance. Renal cysts are believed to arise to failure of communication between convoluted & collecting tubules.

Gross: Both kidneys are enlarged and show numerous small or large cysts containing clear or hemorrhagic (brownish or bluish) fluid. Their lining is smooth. The cysts do not communicate with the renal pelvis. As the patient grows the cysts enlarge and cause pressure atrophy of the renal parenchyma.

Microscopy: Cysts are lined by cuboidal or flattened epithelium.

Complications

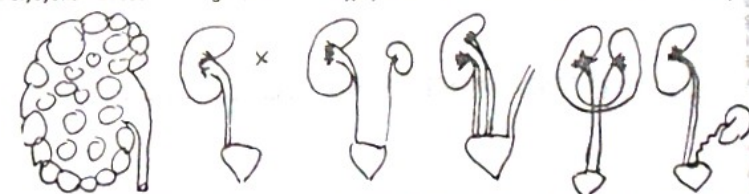
- a) Hematuria
- b) Secondary infection
- c) Hypertension
- d) Chronic renal failure

B Infantile/Childhood Polycystic Disease of the Kidney:

- A rare condition.
- Autosomal recessive inheritance.
- Associated with congenital hepatic fibrosis.
- Renal cystic affection is much more marked than the adult type.
- Death occurs during infancy or childhood due to renal failure

CONGENITAL RENAL ANOMALIES

Polycystic disease Agenesis Hypoplasia Double ureter Horse shoe Ectopic



enumerate & discuss
= discuss
Congenital polycystic kidney



* disease of heart
* disease of lung
* disease of kidney
* disease of liver
= both kidneys

Any chronic renal disease
 Complicat → @ renal failure
 → 2nd Hypertension

GLOMERULAR DISEASES (GLOMERULONEPHRITIS)

Histological Patterns of Glomerular Affection:

- 1-Diffuse: All glomeruli are affected. Glomerular affection is almost global.
- 2-Focal: Some glomeruli are affected (global or segmental), others are intact.
 - a) Global Affection: Whole capillary tuft is affected.
 - b) Segmental Affection: Only a portion of the capillary tuft is affected.

Types of Glomerulonephritis (GN)

- 1-Primary GN: The disease mainly affects the kidneys
- 2-Secondary GN: kidneys are affected as a part of another disease as SLE, hypertension, diabetes mellitus.

ACUTE DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS (POST-STREPTOCOCCAL GLOMERULONEPHRITIS)

AETIOLOGY AND PATHOGENESIS:

- It is an immune complex disease affecting children and young adults.
- It starts as an upper respiratory infection with nephritogenic strains of group A beta hemolytic streptococci.
- Within 1-4 weeks antibodies are formed & combine with streptococcal antigens → immune complexes. These immune complexes are deposited on the basement membranes of glomerular capillaries → complement activation → destruction of glomerular capillaries by:
 - a) Lytic effect of the complement
 - b) Attraction of neutrophils & release of their proteolytic enzymes.

PATHOLOGICAL FEATURES:

Gross: Mild bilateral kidney enlargement. Cortical oedema & petechial hemorrhages may be seen.

Microscopy:

- a) Glomeruli are enlarged and show:
 - 1) Proliferation of epithelial, endothelial and mesangial cells.
 - 2) Several neutrophils in the glomerular capillaries.
 - 3) Bowman's capsular space shows neutrophils, erythrocytes and some albumin.
- b) Tubules show cloudy swelling and casts (mainly blood casts).
- c) Interstitium: Oedema and neutrophils.
- d) Electron Microscopy (E.M): "Bumpy-lumpy" immune complex deposits, subepithelial, between podocytes & basement membrane.
- e) Immunofluorescence: The deposits consist of IgG, IgM and complement.

Clinical & General Manifestations:

- a) Fever & rigors.
- b) Nephritic syndrome is the classic presentation. It consists of:
 - Hematuria, oliguria, mild proteinuria, hypertension and:
 - Nephritic oedema (starts in lids, particularly in the morning, then may become generalized).
- c) Urine analysis:
 - Oliguria
 - Hematuria. Urine appears dark (Coca cola like) due to altered blood
 - Mild proteinuria
 - High specific gravity (1035)
 - Contain casts (mainly hyaline & blood casts)
- d) Blood analysis: a) Mid rise of urea and creatinine b) Mild anemia
- e) Hypertension

* Any clinical picture = FAHMA
 fever, anemia, hypertension, hematuria, oliguria

تشمس الكلى
 على حسب الشدة المرضية

Aetiology
 idiopathic or autoimmune

VIP + Case

nephritic N Syndrome

cloudy swelling

morning lid nephritic edema



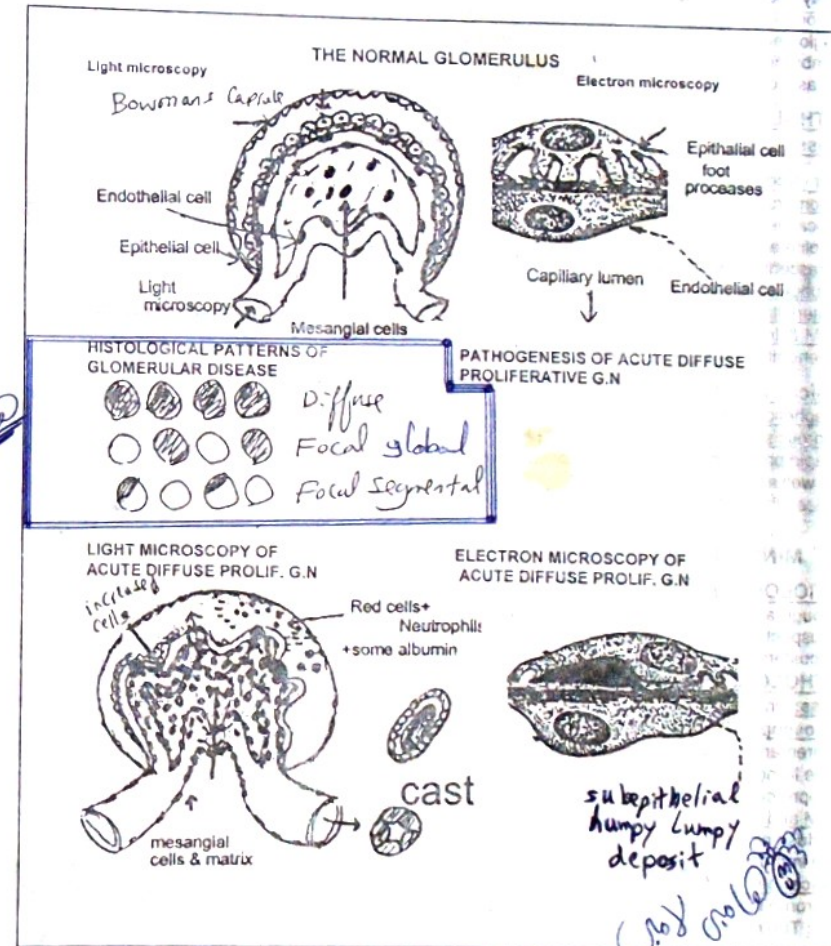
Urine
 CoCo Cola
 Like

Course & Fate:

- a- Recovery in more than 95% of children and in two thirds of adults.
- b- Development of rapidly progressive GN or chronic GN 5%.
- c- rarely death from acute renal failure.

REMARK: URINARY CASTS:

- These are solid urinary constituents detected in urine as cylindrical bodies:
- 1- Hyaline casts consist of protein (in cases of proteinuria).
 - 2- Blood casts consist of blood cells (in cases of hematuria).
 - 3- Cellular casts consist of degenerated detached tubular epithelial cells or inflammatory cells.
 - 4- Granular casts consist of debris.



White Knight

RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (CRESCENTIC GLOMERULONEPHRITIS)

A severe type of diffuse GN. It is termed rapidly progressive due to rapid progression to renal failure. It is also termed crescentic GN due to a characteristic microscopic development of cellular crescents.

AETIOLOGY AND PATHOGENESIS: One of the following possibilities:

- May follow acute diffuse proliferative G. N.
- Idiopathic type** (unknown pathogenesis).
- May be a part of **Goodpasture's syndrome** (Rapidly progressive G.N + pulmonary hemorrhages). It is an autoimmune disease characterized by glomerular lesions caused by anti-glomerular basement membrane antibodies which cross react with alveolar basement membranes causing pulmonary lesions in addition to the glomerular lesions.
- In association with systemic disease as SLE and Henoch-Shonlein purpura.

PATHOLOGICAL FEATURES:

Gross: Bilateral kidney enlargement with cortical oedema & petechial hemorrhages.

Microscopy:

- Glomeruli are enlarged and show:
 - Focal necrosis & capillary thrombosis.
 - Proliferation of mesangial and endothelial cells.
 - Crescents which consist of proliferated parietal epithelial cells, monocytes and fibrin.
- Tubules show cloudy swelling and casts.
- Interstitial inflammatory cells.
- E.M & Immunofluorescence:** Linear deposits of IgG along the glomerular basement membrane (subendothelial).

Clinical manifestations, course and Fate:

- Nephritic syndrome** (hematuria, oliguria, mild proteinuria, hypertension and nephritic oedema) or **nephrotic syndrome** (massive proteinuria, hypoproteinemia, hyperlipemia & generalized oedema).
- Rapid progression to acute renal failure manifested by oliguria, rise of blood urea and creatinine as well as other manifestations (see acute renal failure at end of this chapter).
- Cases that survive longer develop chronic glomerulonephritis.

MINIMAL CHANGE GLOMERULONEPHRITIS (LIPOID NEPHROSIS)

AETIOLOGY AND PATHOGENESIS: Children are affected. Aetiology is unknown. Although antibodies or complement are not detected in the glomeruli, still an immune mechanism is suspected because a) Many cases follow respiratory infections b) Excellent response to corticosteroids.

PATHOLOGICAL FEATURES:

Gross: Unremarkable changes.

Microscopy:

- Unremarkable light microscopic glomerular changes.
- The lining cells of the proximal convoluted tubules may show lipids (due to reabsorption of lipoproteins leaked from the glomeruli).
- E.M and Immunofluorescence:**
 - Diffuse effacement of the foot processes of the visceral epithelial cells.
 - No immunoglobulin deposits.

Clinical picture: Nephrotic syndrome (Minimal change GN is the commonest cause of nephrotic syndrome in children).

Fate: The prognosis is usually excellent; most cases are cured by corticosteroid therapy.

VIP+ (A) K&P

V. Severe

Gross M. U. - glomerulonephritis is seen
Microscopy - crescent

(A)

Def. Commonest cause of nephrotic syndrome in children

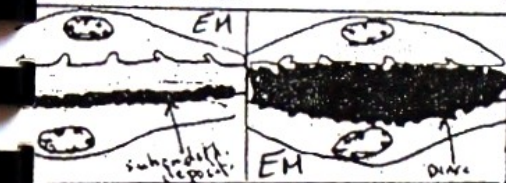
Commonest cause of nephrotic syndrome in Adult =

CRESCENTIC GN



Linear Subendothelial deposits

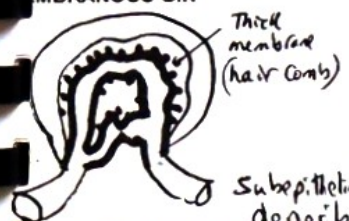
MEMBRANOPROLIF. GN



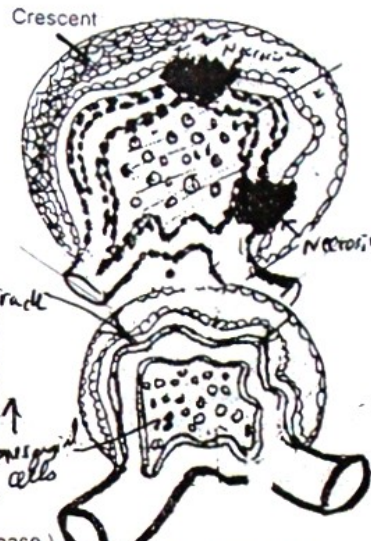
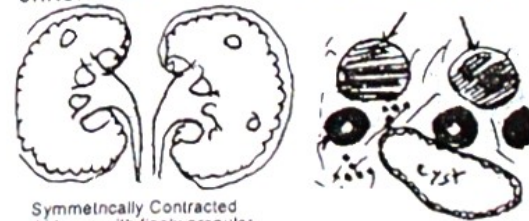
TYPE I
(subendothelial)
MEMBRANOUS G.N

TYPE II
Dense deposit disease
MINIMAL CHANGE GN

FOCAL SEGMENTAL GN



CHRONIC END STAGE KIDNEY glomerular fibrosis



MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN) (also called MESANGIOCAPILLARY G.N)

AETIOLOGY AND PATHOGENESIS:

Children or adults. Unsettled aetiology. May be post infection.

PATHOLOGICAL FEATURES:

Gross: Bilaterally enlarged and pale kidneys.

Microscopy: Glomeruli are enlarged and show:

- Proliferation of mesangial cells and increase in mesangial matrix.
- Thickening of capillary basement membranes which appear double contoured "tram-track appearance".

c) E.M and Immunofluorescence:

- Type I MPGN: Subendothelial deposits of IgG, M and complement.

- Type II MPGN (Dense Deposits Disease or Alternate Pathway Disease): The glomerular

basement membrane shows dense deposits of complement.

Clinical Picture: Nephritic, nephrotic or combined syndromes.

Fate: Unfavorable prognosis; chronic renal failure develops within 10 years in 50% of cases.

MEMBRANOUS GLOMERULONEPHRITIS (MGN)

AETIOLOGY AND PATHOGENESIS: Adults are affected:

- Idiopathic type (85%)
- Secondary type occurring in association with:
 - Infections as malaria, hepatitis B, schistosomiasis mansonii
 - Carcinoma
 - SLE
 - some drugs (as mercury gold and penicillamine)
 - Diabetes

PATHOLOGICAL FEATURES:

Gross: Bilaterally enlarged pale kidneys.

Microscopy:

- Glomerular capillary basement membranes are thickened and may exhibit hair comb appearance of the outer part of the membrane due to immunoglobulin deposition.

b) E.M and Immunofluorescence: Subepithelial deposits of IgG.

Clinical picture: Nephrotic Syndrome.

Fate: Chronic renal failure develops in 50% of cases of idiopathic MGN within 2 to 20 years.

FOCAL PROLIFERATIVE GLOMERULONEPHRITIS

AETIOLOGY AND PATHOGENESIS:

- Idiopathic (unknown aetiology)
- In association with SLE, Goodpasture syndrome, Henoch-Schonlein purpura, subacute bacterial endocarditis. Some cases may follow upper respiratory infections.

PATHOLOGICAL FEATURES:

Gross: Slight bilateral kidney enlargement.

Microscopy:

- Some glomeruli show basement membrane thickening and mesangial cell proliferation.

b) E.M and Immunofluorescence: IgM deposits may be seen.

Clinical picture: Nephrotic syndrome.

Fate:

- May progress to diffuse GN because focal GN may just represent an early phase of a disease that can affect all glomeruli e.g. SLE.
- Development of chronic renal failure in 50% of cases.

FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSG)

AETIOLOGY AND PATHOGENESIS:

- Idiopathic affecting children
- Secondary e.g. heroin abuse.

PATHOLOGICAL FEATURES:

Gross: Slight renal enlargement.

Microscopy:

- Focal hyalinosis and sclerosis of juxtamedullary glomeruli.
- E.M and Immunofluorescence: Mesangial deposits of IgM and complement.

Clinical picture: Nephrotic syndrome.

Fate: Chronic renal failure in 50% of cases.

DIFFUSE MESANGIAL PROLIFERATIVE G.N

AETIOLOGY:

- Idiopathic.
- Schonlein-Henoch's purpura.
- SLE.
- IgA nephropathy (Berger's disease).

PATHOLOGY:

Gross: Mild kidney enlargement.

Microscopy:

- The glomeruli show increased mesangial cells and mesangial matrix.

b) E.M Mesangial dense deposits

c) Immunofluorescence: 1) Mesangial deposits of IgG and C3 are detected. In case of Berger's disease, IgA and C3 are detected.

Clinical: Nephritic syndrome. Hematuria may be prominent.

Fate: Some cases resolve, others progress to renal failure.

LUPUS NEPHRITIS

There are five patterns of renal involvement in systemic lupus erythematosus (SLE)

More than one pattern may coexist). These patterns (classes) include:

- Class I:** Normal microscopic pattern (rare)
- Class II:** Mesangial lupus nephritis: Mild increase of mesangial matrix & mesangial cells of the glomeruli. Mesangial deposits of IgG & C3 are detected. Clinical symptoms are mild.
- Class III:** Focal proliferative glomerulonephritis. Focal means affection of < 50% of glomeruli (or < 50% of the total glomerular capillaries. Clinically: Nephrotic syndrome in 30% of cases
- Class IV:** Diffuse proliferative glomerulonephritis. Diffuse means affection of > 50% of glomeruli (or > 50% of the total glomerular capillaries. This is the most common & most severe form. All glomeruli show diffuse mesangial hypercellularity, commonly with thickening of capillary loops due to fibrinoid necrosis (Wire Loop Lesions). Crescentic lesions may also develop. Clinical effects include nephrotic syndrome (50%). Renal failure ultimately develops.
- Class V:** Membranous glomerulonephritis characterized by thickening of glomerular capillary basement membranes without cellular proliferation. Clinically; nephrotic syndrome

OTHER TYPES OF GLOMERULONEPHRITIS

- Diabetic nephropathy:** See endocrine diseases
- Glomerulonephritis associated with systemic vasculitis**
 - Polyarteritis nodosa
 - Wegener's granulomatosis.
 - Henoch-Schonlein purpura:
- Glomerular diseases associated with Disseminated Intravascular Coagulation**
 - Nephritis in toxemia of pregnancy
 - Hemolytic uremic syndrome:

(A) + VIP + Case + slide

→ End stage kidney

CHRONIC DIFFUSE GLOMERULONEPHRITIS (CHRONIC END STAGE KIDNEY)

AETIOLOGY: End stage of most types of glomerular disease.

PATHOLOGICAL FEATURES:

Gross:

- 1-Both kidneys are symmetrically contracted
- 2-Finely granular surface. = irregular outer surface
- 3-Adherent capsule that strips difficultly with decortication.
- 4-Cut section shows: a) Atrophic cortex and medulla not demarcated from each other.
- b) Increased peripelvic fat c) Prominent vessels and few cysts.

Microscopy:

- 1-Most glomeruli are fibrosed hyalinized and shrunken.
- 2-Atrophic tubules but some show compensatory cystic dilatation.
- 3-Thickened arterioles (Endarteritis obliterans). ***
- 4-Interstitial chronic inflammatory cells and fibrosis.

Clinical Features And Fate: Clinical manifestations & death in chronic renal disease include:

- 1-Hypertension (with all its effects as heart failure, cerebral hemorrhage, retinopathy...etc)
- 2-Chronic renal failure (with all its manifestations as polyuria, blood changes including rise of urea and creatinine and anemia)

Not disease But end of disease

*Complication = failure
2 = hypertension

MAJOR RENAL SYNDROMES

1-Acute nephritic syndrome:

- Characterized by hematuria, oliguria, mild proteinuria, hypertension & oedema of eye lids.
- It is the classic presentation of acute post-streptococcal glomerulonephritis (GN).

2011 define nephritic or nephrotic and discuss one of causes

2-Nephrotic syndrome

It is characterized by:

- a) Massive proteinuria (over 3.5 gm/day)
- b) Hypoalbuminemia (plasma albumin level is less than 3 g%)
- c) Severe generalized oedema due to lowered plasma osmotic pressure
- d) Hyperlipidemia, and lipiduria (lipid in the urine).

Causes of nephrotic syndrome include:

a) Primary Glomerular Disease as:

- Minimal change glomerulonephritis
- Membranous glomerulonephritis
- Mesangiocapillary glomerulonephritis
- Focal proliferative glomerulonephritis
- Focal segmental glomerulosclerosis

b) Secondary glomerular disease as:

- Renal amyloidosis
- Lupus nephritis
- Diabetic glomerulosclerosis

↓ Lipid ↑ Lipid

3-Renal Failure (uremia): Acute and chronic types (see later)

4-Others:

- a) Hematuria with or without proteinuria
- b) Renal tubular defects manifested by polyuria & electrolyte disorders (e.g. metabolic acidosis).
- c) Urinary tract infection is characterized by pyuria (pus in urine)
- d) Renal stones: → renal colic & hematuria
- e) Manifestations of urinary tract obstruction (e.g hydronephrosis)
- f) Manifestations of renal tumors as loin swelling, hematuria, metastases..

DISEASES OF TUBULES AND INTERSTITIUM

ACUTE TUBULAR NECROSIS (*)

AETIOLOGY:

1- **Ischemic necrosis** due to:

- a) Shock due to severe hemorrhage, incompatible blood transfusion, burns...
- b) Rejection after renal transplantation.

2- **Toxic necrosis** caused by carbon tetrachloride, mercury, arsenic...

GROSS: Enlarged kidneys with pale necrotic cortex and congested medulla.

MICROSCOPY:

- 1-Necrosis of tubular epithelium affects the proximal tubules diffusely in case of toxic necrosis. In case of ischemic necrosis, several parts of all tubules are affected associated with basement membrane disruption.
- 2-Occlusion of tubular lumens by granular or epithelial casts.
- 3-Interstitial hyperemia, oedema and inflammatory cells.

EFFECTS AND FATE:

1- **Oligo-anuria** due to reduced glomerular filtration.

Mechanism:

- a) Decreased glomerular perfusion in case of ischemic necrosis.
- b) Vasoconstriction of preglomerular arterioles by chemical substances released due to tubular damage. This results in reduced glomerular filtration.
- c) Obstruction of tubular lumens by swollen or detached necrotic cells.
- d) Fluid leakage from the damaged tubules into interstitial tissue.

• **Death is common** due to a) acute renal failure b) acute heart failure (due to hyperkalemia)

2-Marked polyuria occurs when glomeruli start to function while the unregenerated tubules are incapable of reabsorbing water and electrolytes. Hypokalemia may be a problem at this phase.

3-Restoration of renal functions occurs after tubular regeneration.

VSA + G/K + J + (A)

PYELONEPHRITIS

DEFINITION: Infection of kidney (interstitial tissue) & renal pelvis.

AETIOLOGY:

Predisposing factors:

- 1-Low immunity as in cases of
 - a) Diabetes mellitus
 - b) AIDS
 - c) immunosuppressive therapy
- 2-Urinary obstruction (by stones, tumors, strictures...etc) . Stasis of urine favors bacterial growth.
- 3-Females are commonly affected than males because of:
 - a) Shorter wider urethra (easier infection).
 - b) Pregnancy: this leads to urinary stasis.
- 4-Urinary tract instrumentation e.g. Catheterization

Bacteria: E. coli (commonest), Staphylococci, Streptococci, Pseudomonas, Typhoid bacilli & others.

Routes:

- 1-Heamatogenous (blood spread from distant infections as those of respiratory tract).
- 2-Ascending (through periureteric lymphatics or submucosa of ureter).
- 3-From colon through intercommunicating lymphatics.

PATHOLOGY: Two types. Commonly bilateral:

① Co = staph + strep
② Mo = ① descending (haematogenous)
② Ascending (urinary tract)
③ From Colon (lymphatic)

VIP+A+Case+Gp

Kidney is commonly both kidneys

ACUTE PYELONEPHRITIS	CHRONIC PYELONEPHRITIS
GROSS PICTURES	
1-Enlarged kidneys. 2-Smooth surface. 3-Capsule: Strips easily. 4-Cutsection: Small cortical abscesses + streaks of pus along medullary rays. 5-Pelvis and calyces contain pus.	1-Asymmetrically contracted kidneys. <i>Shrunken size</i> 2-Irregular surface depressions (scars). 3-capsule: Adherent. 4-Cutsection: Scarred cortex and medulla not demarcated from each other. 5-Scarred distorted pelvis and calyces. <i>6-increased papillary fat</i>
MICROSCOPIC FEATURES	
1-Interstitium of kidney and pelvis: a) Dilated capillaries. b) Neutrophils, pus cells and macrophages (abscesses). c) Oedema. 2-Tubules: degeneration, inflammation and leucocytic casts.	1-Interstitium of kidney and pelvis: a) Endarteritis obliterans. b) Lymphocytes, plasma cells, macrophages. c) Fibrosis. It may surround the glomeruli (periglomerular) leading to glomerular ischemia ending with glomerular fibrosis. 2-Tubules: a) Some are fibrotic. b) Some are cystic c) Some contain thyroid-like (colloid) casts.
FATE AND COMPLICATIONS	
1-Mild cases: Recovery. 2-Severe cases: Acute renal failure. 3-Some cases develop pyonephrosis or progress to chronic pyelonephritis.	1-Hypertension. <i>= 2nd type</i> 2-Chronic renal failure.

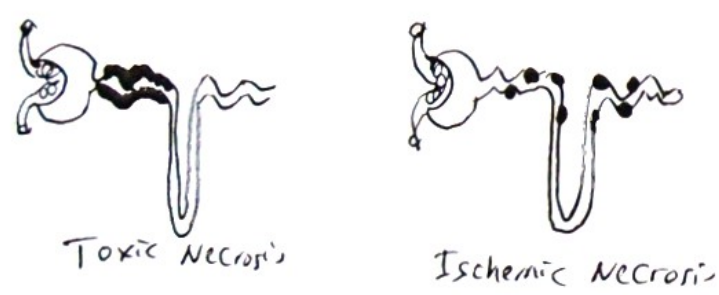
(X) TYPES OF TUBULO-INTERSTITIAL NEPHRITIS

- 1-Infective as pyelonephritis, tuberculosis, bilharziasis & xanthogranulomatous pyelonephritis.
- 2-Non-infectious (called interstitial nephritis) e.g. drug induced.

Xanthogranulomatous Pyelonephritis:
Characterized by foam macrophages, giant cells & granulomas. Often caused by E coli infection.

Drug Induced Interstitial Nephritis:
Acute allergic inflammation caused by some drugs as non-steroidal anti-inflammatory drugs. The interstitial tissue is markedly infiltrated by chronic inflammatory cells & eosinophils. The urine shows proteinuria and hematuria. Eosinophilia is common. Acute tubular necrosis may occur in severe cases

ACUTE TUBULAR NECROSIS



Freely you have received; freely give.

ACUTE PYELONEPHRITIS

easily stripping capsule

Abscess

CHRONIC PYELONEPHRITIS

Thick

No demarcation

Asymmetrical irregular contraction

How to differentiate between pyonephrosis & hydronephrosis?

→ by adhesion, if fibrotic & fixed = pyonephrosis

pus kidney condition

PYONEPHROSIS

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with pus → atrophy of renal tissue.

AETIOLOGY:
1-Pyelonephritis associated with urinary tract obstruction
2-Urinary tract obstruction (hydronephrosis) followed by 2ry infection

PATHOLOGY:
1-Pelvis and calyces are distended with pus.
2-Atrophic renal tissue.
3-Spread of infection to surroundings (perinephritis) → fibrosis & fixation of kidney.
4-Chronic renal failure in bilateral cases.

Complications
① renal failure
② 2nd hypertension
③ Amyloidosis

HYDRONEPHROSIS

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with urine due to urinary obstruction, followed by pressure atrophy of renal tissue.

AETIOLOGY: Incomplete or intermittent urinary tract obstruction.

White Knightstone

VIP + A + Case + USK

Kidney diseases commonly both kidneys

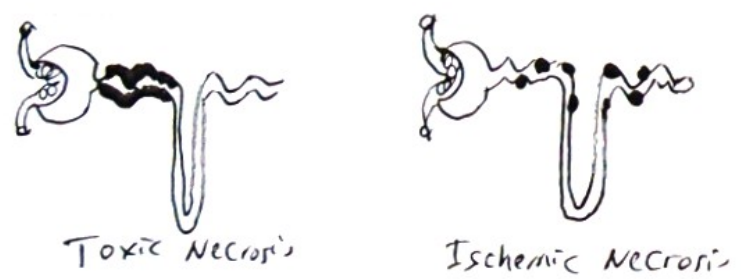
ACUTE PYELONEPHRITIS	CHRONIC PYELONEPHRITIS
GROSS PICTURES	
1-Enlarged kidneys. 2-Smooth surface. 3-Capsule: Strips easily. 4-Cutsection: Small cortical abscesses + streaks of pus along medullary rays. 5-Pelvis and calyces contain pus.	1-Asymmetrically contracted kidneys. <i>shrunken size</i> 2-Irregular surface depressions (scars). 3-capsule: Adherent. 4-Cutsection: Scarred cortex and medulla not demarcated from each other. 5-Scarred distorted pelvis and calyces. <i>6-increased pericyclic fat</i>
MICROSCOPIC FEATURES	
1-Interstitium of kidney and pelvis: a) Dilated capillaries. b) Neutrophils, pus cells and macrophages (abscesses). c) Oedema. 2-Tubules: degeneration, inflammation and leucocytic casts.	1-Interstitium of kidney and pelvis: a) Endarteritis obliterans. b) Lymphocytes, plasma cells, macrophages. c) Fibrosis. It may surround the glomeruli (periglomerular) leading to glomerular ischemia ending with glomerular fibrosis. 2-Tubules: a) Some are fibrotic. b) Some are cystic c) Some contain thyroid-like (colloid) casts.
FATE AND COMPLICATIONS	
1-Mild cases: Recovery. 2-Severe cases: Acute renal failure. 3-Some cases develop pyonephrosis or progress to chronic pyelonephritis.	1-Hypertension. <i>= 2° type</i> 2-Chronic renal failure.

(X) TYPES OF TUBULO-INTERSTITIAL NEPHRITIS

- 1-Infective as pyelonephritis, tuberculosis, bilharziasis & xanthogranulomatous pyelonephritis.
- 2-Non-infectious (called interstitial nephritis) e.g. drug induced.

Xanthogranulomatous Pyelonephritis:
Characterized by foam macrophages, giant cells & granulomas. Often caused by E coli infection.
Drug Induced Interstitial Nephritis:
Acute allergic inflammation caused by some drugs as non-steroidal anti-inflammatory drugs. The interstitial tissue is markedly infiltrated by chronic inflammatory cells & eosinophils. The urine shows proteinuria and hematuria. Eosinophilia is common. Acute tubular necrosis may occur in severe cases

ACUTE TUBULAR NECROSIS



ACUTE PYELONEPHRITIS

CHRONIC PYELONEPHRITIS

How to differentiate between pyonephrosis & hydronephrosis?
→ by adhesion, if fibrotic & fixed = pyonephrosis

acute pyelonephritis specially for & Comp **PYONEPHROSIS**

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with pus → atrophy of renal tissue.

AETIOLOGY:
1-Pyelonephritis associated with urinary tract obstruction
2-Urinary tract obstruction (hydronephrosis) followed by 2ry infection

PATHOLOGY:
1-Pelvis and calyces are distended with pus.
2-Atrophic renal tissue.
3-Spread of infection to surroundings (perinephritis) → fibrosis & fixation of kidney.
4-Chronic renal failure in bilateral cases.

Complications
① renal failure
② 2° hypertension
③ Amyloidosis

Hydronephrosis

DEFINITION: A chronic condition in which pelvis and calyces are markedly distended with urine due to urinary obstruction, followed by pressure atrophy of renal tissue.

AETIOLOGY: Incomplete or intermittent urinary tract obstruction.

Water longstone

Aetiology of Hydronephrosis = I

This may be due to:

1-Urethral Lesions: These may be:

a) Congenital lesions

- Phimosis (stenosis of opening of the prepuce of penis)
- Stenosis of external urethral meatus
- Prostatic urethral valves

b) Acquired causes:

- Post traumatic or post inflammatory urethral stricture
- Urethral tumors.

2-Prostatic Enlargement:

- a) Senile enlargement.
- b) Carcinoma.

3-Bladder Neck Obstruction:

- a) Functional neuromuscular incoordination as in tabes dorsalis.
- b) Inflammatory stricture as bilharzial fibrosis.
- c) Tumors
- d) Stone

4-Ureteric Lesions:

- a) Inflammatory stricture as bilharzial fibrosis.
- b) Stone.
- c) Tumors.
- d) Pregnancy
- e) Retroperitoneal fibrosis

5-Renal Pelvis:

- a) Stone
- b) Tumors.
- c) Pressure by an aberrant renal artery
- d) Kinked pelvis and ureter.

PATHOLOGY:

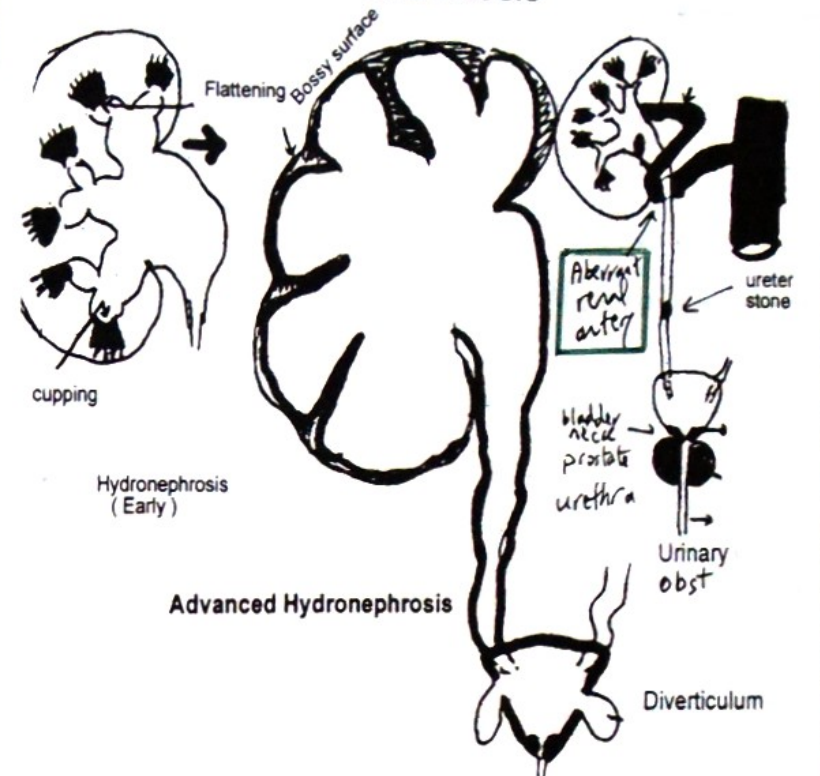
- Hydronephrosis may be unilateral due to unilateral ureteric or pelvic lesions = above bladder
- It may be bilateral due to urethral, prostatic or bladder neck lesions = below bladder
- Bilateral hydronephrosis is associated with:
 - Hypertrophy, dilatation & trabeculation of the bladder.
- ★ Bladder diverticula may develop due to pouching of the mucosa through muscle defects after marked bladder dilatation
- Bilateral hydroureter. Ureters appear hypertrophied, dilated, elongated & tortuous.
- Distension of pelvis & calyces with urine → pressure atrophy → flattening, then cupping of pyramids followed by disappearance of the whole pyramids & progressive atrophy of renal parenchyma.
- Gross: The affected kidney is enlarged with bossy surface. Cut section reveals a multilocular sac distended with urine.

COMPLICATIONS:

- 1-Secondary infection → pyonephrosis.
- 2-Hypertension.
- 3-Stasis. This predisposes to stone formation.
- 4-Chronic renal failure in bilateral cases.
- 5-Bladder diverticula may be complicated by secondary infection, stone formation and carcinoma.

Hydronephrosis
= Obstructive neuropathy

HYDRONEPHROSIS



VASCULAR DISEASES OF THE KIDNEY (x)

- 1-Infarction: see general pathology
- 2-Benign and malignant nephrosclerosis (arteriolosclerotic kidney): see hypertension
- 3-Senile renal atrophy: Atherosclerotic ischemic atrophy of kidneys in old age.
- 4-Bilateral cortical necrosis may occur due to severe shock or in cases of toxemia of pregnancy. It is manifested by acute renal failure & is rapidly fatal.

URINARY CALCULI (STONES) (UROLITHIASIS)

VIF + A + Case - 20

They are due to precipitation of urinary crystalloids in renal pelvis or in the bladder.

AETIOLOGY:

1- Disturbances Of Composition Of Urine:

- a) Decreased water content (concentrated urine) e.g. due to excessive sweating.
- b) Increased crystalloids:
 - Excess calcium as in hyperparathyroidism.
 - Excess uric acid and urates in cases of gout.
 - Excess oxalates: 1) hereditary metabolic error 2) excess intake in diet (mango, tomato..).
 - Familial Cystinuria.

gall stones 20 5 12

stasis
↓
crystals
↓
stones

2-Stasis Of Urine due to urinary obstruction

- Stasis allows easier precipitation of the crystalloids of urine.
- Stasis predisposes to infection.

3-Urinary Infection: It predisposes to precipitation of urinary crystalloids through:

- Formation of a nucleus (pus cells, detached necrotic cells);
- Change of pH of urine:
 - Alkalinity (in case of pyogenic bacteria). Precipitation of calcium-magnesium-ammonium phosphate (Triple Phosphate Stone), occurs in alkaline urine.
 - Increased Acidity (in case of E. coli). This favors precipitation of oxalates and urates.

TYPES OF STONES:

Mostly Multiple stone
1-Primary (Metabolic) Stones: Urinary infection is not essential for their formation:

- Calcium Oxalate Stone (60%):** It forms in acidic urine. Usually occurs in renal pelvis and is multiple, hard with spiny surface. This leads to injury of urinary mucosa and hemorrhage which leads to dark staining of the stones.
- Uric Acid and Urate Stones (8%):** It forms in acidic urine. Usually occurs in renal pelvis and is single, hard, has a smooth surface and yellowish brown in colour.
- Cystine Stones (2%):** Soft, yellowish green.

2-Secondary (Infected) Stones: Triple Phosphate Stone (30%). It develops in alkaline urine. Usually single, large white and friable with a smooth surface. It commonly forms in urinary bladder but may form in renal pelvis and calyces; casting their shape (**Stag Horn Stone**).

COMPLICATIONS:

- MIMO = migration + infection + malignancy + obstruction*
- Migration from renal pelvis to ureter or bladder: a) Pain (colic) b) Urinary obstruction.
 - Urinary obstruction leading to hydronephrosis, hydronephrosis and sometimes calculous anuria.
 - Urinary infection (predisposed to by urinary stasis due to obstruction) leading to cystitis, pyelonephritis, pyoureter, pyonephrosis.
 - Injury of urinary mucosa (particularly by oxalate stone). This leads to hematuria.
 - Squamous Metaplasia. Squamous cell carcinoma may occur on top of metaplasia.

URINARY CALCULI



surface is rough;
colour brown,

Calcium oxalate



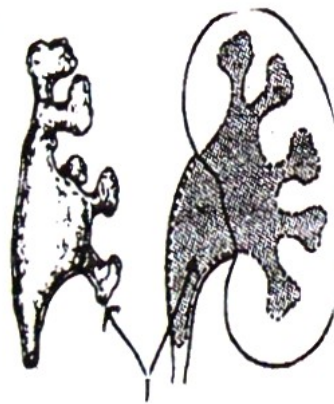
Smooth
light brown
colour

Uric acid and urates



grayish
white

phosphate



Staghorn calculus

TUMORS OF KIDNEY & RENAL PELVIS

SECONDARY (METASTATIC) TUMORS:

These are uncommon tumors which may reach the kidney by
 1-Blood spread from distant malignant tumors and from myeloma and leukemia
 2-Direct or lymphatic spread from adrenal glands, pancreas & colon.

PRIMARY TUMORS:

1-Tumors of Pelvis:

A) Benign Tumors:

- Villous papilloma & inverted papilloma. May cause hematuria.
- Hemangioma (capillary or cavernous). May cause hematuria
- Leiomyoma, neurofibroma

B) Malignant Tumors:

- Transitional cell carcinoma
- Squamous cell carcinoma

2-Tumors of Kidney:

A) Benign Renal Tumors:

- Cortical Adenoma:** It is a benign tumor which appears as a well circumscribed, round, yellowish nodule in the cortex., usually 2 cm or less in diameter. It may change into carcinoma.
- Oncocytoma:** It is a benign tumor derived from proximal tubular cells and may reach a large size. Microscopically, it consists of proliferating epithelial cells having eosinophilic cytoplasm (oncocytes).
- Angiomyolipoma:** A capsular hamartoma which may reach large size, composed of mature adipose tissue, smooth muscle cells and abnormal blood vessels. Usually occurs in association with tuberous sclerosis (epilepsy, mental retardation & sebaceous adenoma of skin).
- Medullary fibroma.**
- Juxta-glomerular cell tumor:** It is a renin secreting tumor leading to hypertension.
- Others:** as hemangioma, lymphangioma, lipoma ...

B) Malignant Renal Tumors:

- Wilm's tumor (Nephroblastoma, Embryoma).
- Renal cell carcinoma (hypernephroma).
- Sarcomas & lymphoma

RENAL CELL CARCINOMA (HYPERNEPHROMA)

Renal cell carcinoma (RCC) accounts for about 3% of adult malignancy. Men are affected more than women. The peak incidence is in the sixth decade of life.

Gross appearance:

- Most tumors arise in pole of the kidney, upper or lower.
- As the tumor grows it pushes the kidney which may appear crescentic.
- The tumor finally invades the renal parenchyma and renal pelvis
- The tumor usually appears defined & eccentrically located.
- Tumor ranges in length between 2 & >30 cm.
- Cut section is typically bulging and yellowish (due to high lipid & glycogen content of tumor cells). However, the tumor may be whitish or brownish according to microscopic tumor cell type.
- Variable degrees of cystic changes, hemorrhage & necrosis are common.

Microscopic appearance: Variable:

1- Clear cell type:

- This is the most common type.
- Tumor cells show vacuolated cytoplasm (due high content of lipids & glycogen)
- Cell borders are distinct



Case (A) + VISA 0.3-1
might be 50%

Microscopic appearance

- Nuclei appear rounded & small (due to abundance of cytoplasm)
- The cells are arranged in trabeculae and acini.
- 2- **Papillary type:** Tumor cells are small, cuboidal to low columnar forming papillary projections.
- 3- **Granular cell/ chromophobe cell type:** Cells show abundant acidophilic granular cytoplasm.
- 4- **Sarcomatoid type:** least common variant, formed of undifferentiated spindle epithelial cells; thus resembling sarcoma.
- 5- **Collecting duct type:** Very rare subtype, composed of mixture of dilated tubules & papillae lined by a single layer of cuboidal cells associated with desmoplastic stroma.
- 6- **Renal medullary carcinoma:** An extremely rare tumor, centered in the renal medulla, arising in young black patients with sickle cell disease

Spread:

- 1- **Direct:** to renal pelvis, renal vein, perinephric tissue and surrounding structures.
- 2- **Lymphatic:** Para-aortic nodes.
- 3- **Blood:** to lungs (commonly causing cannon ball metastases), bones & others.

Clinical features:

- 1- Painless hematuria
- 2- Loin pain
- 3- Palpable loin mass
- 4- Varicocele of left testis in case of left RCC
- 5- It may remain clinically occult and manifest by metastatic disease.

NEPHROBLASTOMA (WILM'S TUMOR) - embryoma

The commonest embryonic tumor in infancy and childhood. It accounts for 13-20% of malignant tumors (other than Leukemias) in children under 15 years of age. In 6% of cases the tumor is bilateral. One third of tumors are hereditary.

Gross picture:

- Most tumors are large.
- Cut surface is demarcated, noncapsulated, whitish & bulging, giving encephaloid appearance.
- Hemorrhage, cystic changes & necrosis are common.

Microscopic picture: Classically the tumor is triphasic & consists of:

- Small undifferentiated **blastemal** cells usually in aggregates.
- **Epithelial** cells arranged in ribbons, primitive tubules or glomeruloid structures
- **Mesenchymal** elements which may be undifferentiated or show muscle or cartilaginous differentiation.

Spread:

- 1- Direct to perinephric tissue and surrounding structures.
- 2- Lymphatic: Para-aortic nodes.
- 3- Blood: Lungs, bone, others.

STAGING OF RENAL TUMORS

Staging of RCC (TNM Staging):

- T1 Tumor limited to kidney ≤ 7 cm
 T2 Tumor limited to kidney > 7 cm
 T3a Perinephric or adrenal gland invasion.
 T3b Invasion of renal vein or vena cava
 T3c Extension to vena cava above diaphragm
 T4 Tumor invades beyond Gerota fascia.
 N0: Negative nodes N1 single node N2 2 or more
 M0: no distant metastases M1 distant metastases

Staging of Wilm's Tumor:

- Stage I: Limited to kidney, completely resected.
 Stage II: Invasion beyond kidney, but completely resected.
 Stage III: Residual nonhematogenous tumor confined to abdomen
 Stage IV: Hematogenous metastases.
 Stage V: Bilateral renal involvement at diagnosis.

RENAL CELL CARCINOMA

(RCC)

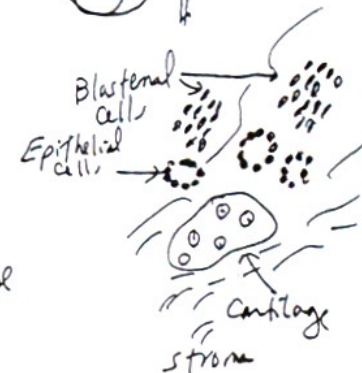


Crescentic kidney
compressed
at one pole

RCC
clear
cell type



WILM'S TUMOR



RENAL FAILURE (URAEimia)

(B) + Case + Gp

DEFINITION: This is failure of kidneys to eliminate into urine the toxic compounds that normally exist in blood (waste metabolic products).

TYPES AND CAUSES:

1-Acute Renal Failure: Due to: die in 48 hours due to pulmonary oedema

- **Pre-renal** causes as shock e.g. due to burns or hemorrhage.
- **Renal** causes as acute tubular necrosis, acute pyelonephritis, acute G.N.
- **Post-renal** causes: Calculus anuria due to sudden ureteric obstruction by a stone.

2-Chronic Renal Failure: Due to chronic bilateral kidney disease as:

- Amyloidosis.
- Chronic pyelonephritis.
- Chronic glomerulonephritis.
- Hydronephrosis.
- Pyonephrosis.
- Renal tumors...

PATHOLOGICAL FEATURES:

1- Blood Changes:

- Rise of urea, creatinine and other nonprotein nitrogenous compounds.
- Retention of phosphates and lowering of calcium.
- Retention of sodium and potassium.
- Acidosis.

Anaemia

↑ urea ↑ creatinine ↑ phosphate ↓ Ca⁺⁺
 ↓ Na⁺ ↓ K⁺
 ↓ HCO₃⁻ but no tetany

White Knightstone

* What is cause of Anaemia in renal failure?

- Anaemia due to toxic depression of bone marrow & reduced erythropoietin formation by the kidneys.

2-Urine Volume:

- In case of acute uremia, oligo-anuria is usual.
- In case of chronic uremia: polyuria.

3-Organ Lesions:

- Serous membranes: Fibrinous pleurisy and fibrinous pericarditis.
- Skin is pale (due to anaemia) and shows petechial hemorrhages as well as grayish and brownish discoloration related to urea or urochrome pigment deposition.
- GIT: Glossitis (tongue inflammation), gastritis, enteritis and colitis.
- Lungs: Pulmonary oedema and infections in addition to uremic fibrinous pleurisy.
- Cerebral oedema leading to tremors, convulsions and coma.

RENAL TRANSPLANT REJECTION (X) Microbiology subject

1-HYPERACUTE REJECTION: It occurs within minutes to hours after transplantation. It is due to pre-existing circulating antibodies in the recipient (related to previous pregnancies or blood transfusions). Fibrin thrombi develop in all renal vessels including the glomeruli → infarcts & acute tubular necrosis.

2-ACUTE REJECTION: Occurs any time after transplantation, mostly during the first months following transplantation. Acute rejection is of 2 types:

- Acute Cellular Rejection (Reversible Rejection):** The interstitium is infiltrated by lymphocytes (mostly T cells), plasma cells, immunoblasts, macrophages and some neutrophils
- Acute Vascular Rejection (Irreversible Rejection):** The vascular walls are infiltrated by lymphocytes, macrophages & immunoblasts. Necrotizing fibrinoid and thrombotic lesions may occur. Glomeruli are hypercellular & show endothelial swelling. Infarcts, tubular necrosis & interstitial hemorrhage occur.

3-CHRONIC REJECTION: There is arteriosclerosis, glomerular fibrosis (glomerulosclerosis), diffuse interstitial fibrosis and tubular atrophy, i.e. a picture of end stage kidney.

4-COMPLICATIONS OF IMMUNOSUPPRESSION:

- Cyclosporin toxicity:**
 - Acute toxicity (acute tubular necrosis)
 - Chronic toxicity (interstitial fibrosis)
- Infections & tumors (Kaposi's sarcoma).**

DISEASES OF THE URINARY BLADDER

DIVERTICULA (X)

Definition And Types: Localized pouching of bladder wall. Two types:

- 1-Congenital (true) diverticulum:** Single. Its wall consists of all layers of urinary bladder wall.
- 2-Acquired (false) diverticula:** Usually multiple.
 - Wall consists of mucosa only.
 - Caused by bladder neck obstruction (see before: complications of hydronephrosis)

Complications:

- Secondary infection.
- Stone formation.
- Carcinoma.

CYSTITIS (INFLAMMATION OF BLADDER) (B) + G.P.

1-ACUTE CYSTITIS:

Aetiology: acute inflammation of mucosa of urinary bladder. $C + M + P$ (bacteria, microorganisms, parasites)

Predisposing factors:

- Low immunity (as in diabetics)
- Urine Stasis due to:
 - Urethral or bladder neck obstruction e.g. bilharzial fibrosis, stones, tumors, enlarged prostate
 - Functional abnormalities as in cases of spinal cord injuries & Tabes dorsalis
- Bladder instrumentation (catheterization, cystoscopy).

- The causative bacteria: Staphylococci, streptococci, E coli, gonococci...etc)
- Routes of infection:

- Direct from urethra
- Descending from kidney infections
- Lymphatic from pelvic organs
- Blood spread from distant infections e.g. of lungs and upper respiratory tract.

Clinically: ↑ rate of urination & inability to control urination. Frequency, urgency, dysuria (burning micturition), pyuria (pus in urine) and Hematuria.

Pathology: @ Site: Mucosa of urinary bladder

- Inflammation may be mild.
- Severe inflammation is suppurative, ulcerative & hemorrhagic.
 - Cytological examination of urine shows large numbers of neutrophils and pus cells.
 - Biopsy from the bladder shows picture of acute suppurative inflammation (dilated capillaries, oedema, neutrophils, pus cells & macrophages).
- Rarely membranous inflammation.

Complications:

- Spread of infection
- Chronicity (chronic nonspecific cystitis)

2-CHRONIC NONSPECIFIC CYSTITIS:

Aetiology: May follow acute cystitis or start as low grade chronic inflammation

Clinically: Frequency, dysuria, pyuria & may be hematuria.

Pathology:

- Chronic nonspecific inflammation & fibrosis
- Urothelial changes like those occurring in bilharzial cystitis may occur (see general & describe)

Complications:

- Spread of infection
- Stones
- Contracted bladder due to fibrosis → thumblike bladder
- Leukoplakia and carcinoma.

3-SPECIFIC TYPES OF CYSTITIS

- Granulomatous Cystitis as bilharzial,** tuberculous, fungal & amoebic cystitis.
- Eosinophilic cystitis:** inflammation rich in eosinophils (allergic cystitis).
- Gangrenous cystitis:** A serious type of infective gangrene typically occurring in old debilitated patients.
- Emphysematous Cystitis:** Inflammation, associated with gas produced by bacteria; as A. aerogenes.
- Polypoid Cystitis:** Chronic inflammation with polypoid projections, seen in patients with indwelling catheters.
- Chronic interstitial cystitis (Hunner's ulcer):** Chronic inflammation & mucosal ulceration of unknown cause
- Follicular cystitis:** Chronic cystitis of unknown aetiology in which inflammation is accompanied by lymphoid follicle formation.
- Malakoplakia:** Inflammation of unknown aetiology, characterized by predominance of histiocytes containing intracytoplasmic inclusions called Michaelis-Gutmann bodies. (called Von Hansemann cells).

TUMORS OF THE BLADDER

1) EPITHELIAL BLADDER TUMORS (benign & malignant)

A) UROTHELIAL (TRANSITIONAL) TUMORS:

- Flat lesion:** Urothelial (transitional) cell carcinoma in situ
- Nonpapillary urothelial (transitional) cell carcinoma**
- Papillary lesions:**
 - Inverted papilloma (benign)
 - Villous papilloma (benign)
 - Papillary urothelial tumor of uncertain malignant potential (PUNLMP)

- Papillary carcinoma, low grade
- Papillary carcinoma, high grade
- Micropapillary carcinoma

B) SQUAMOUS TUMORS: Arise on top of squamous metaplasia or from female bladder trigone

- Squamous papilloma (Condyloma): Rare benign lesion
- Squamous carcinoma in situ
- Squamous cell carcinoma
- Verrucous squamous carcinoma

C) GLANDULAR TUMORS: Arise from urachus or on top of glandular metaplasia (cystitis glandularis)

- Villous or tubular adenoma (resembling that of colon): Rare benign lesion
- Adenocarcinoma with or without mucoid activity

II) NONEPITHELIAL BLADDER TUMORS (benign & malignant)

BENIGN: Fibroma, neurofibroma, angioma, leiomyoma, paraganglioma

MALIGNANT:

- a) Sarcomas as leiomyosarcoma, rhabdomyosarcoma, angiosarcoma & others.
- b) Carcino-sarcoma (rare)
- c) Lymphoma.

III) SECONDARY TUMORS

- a) Direct spread from cancer prostate, rectum or uterine cervix
- b) Transluminal implantation from transitional carcinoma of pelvis or ureter.

VILLOUS PAPILOMA (TRANSITIONAL CELL PAPILOMA)

Gross Picture:

- A noncapsulated velvety friable grayish pink mass composed of delicate papillary processes.
- The tumor is commonly single, but may be multiple.

Microscopic Picture: Delicate vascularized connective tissue cores covered by usually not more than six layers of regular transitional cells.

CARCINOMA OF THE URINARY BLADDER

The most common tumor of Egyptian males due to bilharzial cystitis. However it may arise also in non-bilharzial bladder. It is less common in females. In Egypt bladder cancer is of two types:

BILHARZIAL CARCINOMA	NONBILHARZIAL CARCINOMA
AGE	
Relatively younger, 30-50 years.	Usually above age of 50 years.
PREDISPOSING FACTORS	
1-Bilharzial urothelial precancerous lesions as cystitis glandularis, squamous metaplasia, leukoplakia and dysplasia. 2-Cryptophan metabolites released from the worms into the blood & excreted in urine are carcinogenic. 3-Try infection of bilharzial bladder is common. Gram negative bacteria as E. coli change urinary nitrites & nitrates into nitrosamines → carcinogenic particularly to metaplastic urothelium. 4-Superimposed papilloma virus infection	1-Villous papilloma. 2-Chemical carcinogens as aniline dye. 3-Stones leading to squamous metaplasia. 4-Smoking. 5-Ectopia vesica (congenital absence of anterior bladder wall and anterior abdominal wall). 6-Chronic cystitis.
SITES	
Both bilharzial and nonbilharzial carcinoma are common in lateral and posterior walls	
GROSS FEATURES	
* due to severe irritation	

Pathology site
Gross effect + Complication

- 1-PAPILLARY PATTERN (less common).
 2-NON PAPILLARY TYPES (more common):
 a) Fungating polypoid pattern.
 b) Ulcerative pattern (describe).
 c) Infiltrative pattern.

- 1-PAPILLARY PATTERN (common)
 2-NON-PAPILLARY PATTERNS
 a) Fungating pattern.
 b) Ulcerative pattern.
 c) Infiltrative pattern.

MICROSCOPIC FEATURES

- 1-Squamous cell carcinoma (common): classical or rarely verrucous types
 2-Urothelial/ Transitional cell carcinoma (TCC):
 a) Nonpapillary TCC.
 b) Papillary TCC.
 3-Adenocarcinoma (rare).

- 1-Urothelial/transitional carcinoma (commonest):
 a) Papillary TCC (better prognosis)
 b) Nonpapillary TCC (tends to invade deeper than papillary TCC).
 2-Adenocarcinoma (rare).
 3-Squamous cell carcinoma (rare). Classic or Verrucous types

EFFECTS AND COMPLICATIONS

1-Spread:

- Direct: To prostate, seminal vesicles, ureters, rectum, vagina.
- Lymphatic to iliac and para-aortic lymph nodes.
- Blood: To lungs, liver, bone...

Remark: It is believed that distant spread of bilharzial carcinoma is less frequent than nonbilharzial carcinoma due to fibrotic compression of vessels.

2-Urinary Obstruction (hydronephrosis, retention of urine, renal failure).

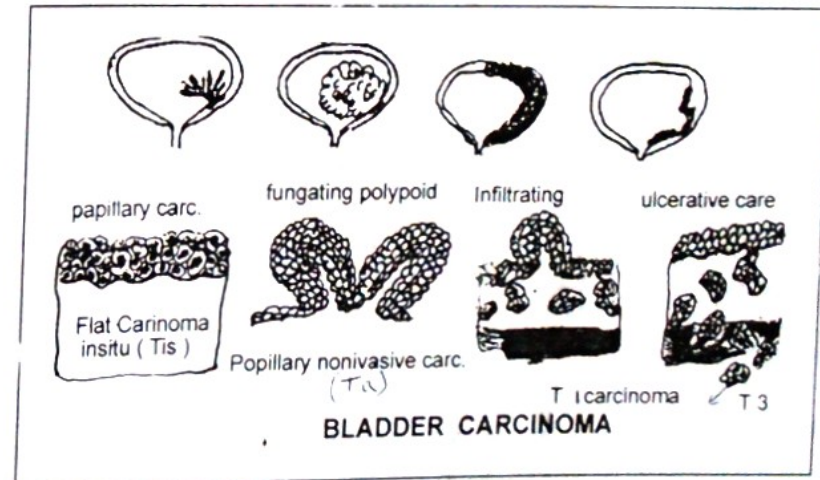
3-Infection (cystitis, pyelonephritis, pyoureter, pyonephrosis).

4-Haematuria.

5-Fistula Formation: with rectum or vagina due to direct spread.

T.N.M. STAGING OF BLADDER CARCINOMA:

T (Tumor)	N (lymph nodes)	M (Distant metastases)
- Tis: Noninvasive flat tumor (carcinoma in situ). - Ta: Noninvasive papillary carcinoma. - T1: Invasion limited to lamina propria. - T2: Invasion of muscularis. - T3: Invasion of perivesical fat - T4: Contiguous spread to adjacent organs.	- N0: negative LN - N1: Single LN < 2 cm - N2: Single LN 2-5 cm or multiple LNs < 5 cm - N3: Any LN > 5 cm.	- M0: No evidence. - M1: Evidence of distant metastases.



BLADDER CARCINOMA

Dyscrasias of blood in urine

HAEMATURIA

VIP + A +
 VIP → 30%
 Urinary bladder carcinoma
 renal cell carcinoma
 nephroblastoma

Aetiology

Blood passing in urine may be due to:

1-PRE-RENAL CAUSES (General causes of bleeding):

- Hypertension
- Blood diseases as leukemia & purpura.
- Vitamin C & K deficiency
- Drugs as salicylates and anticoagulants.

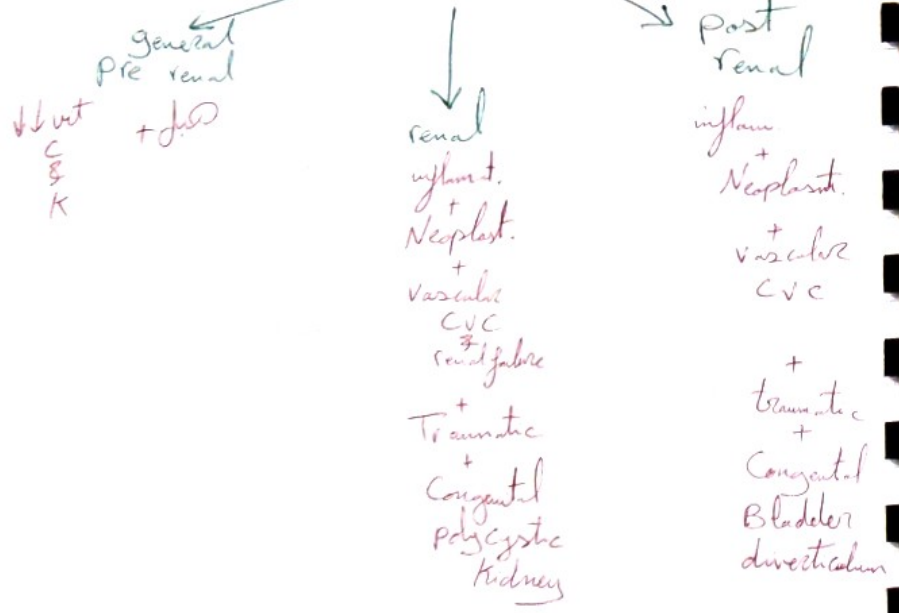
2-RENAL CAUSES: as

- Congenital as polycystic kidney.
- Inflammatory as:
 - Nephritic syndrome (as acute post streptococcal glomerulonephritis).
 - Acute pyelonephritis.
- Neoplastic (renal tumors) as hypernephroma.
- Vascular disorders as: chronic venous congestion and renal infarction.
- Traumatic e.g kidney injury due to accidents and bleeding following renal surgery.

3-POST-RENAL CAUSES:

- Congenital as: Bladder diverticulum.
- Inflammatory as
 - Bilharziasis. This is one of the most common causes of hematuria in Egypt.
 - Other types of cystitis e.g acute cystitis, tuberculous cystitis ... etc
- Neoplastic: Tumors of renal pelvis, ureter or bladder (e.g papilloma, carcinoma...).
- Vascular disorders as chronic venous congestion
- Traumatic as:
 - Traumatic injury by stones. This is a common cause of hematuria
 - Traumatic injury due to instrumentation by metal catheters

Haematuria Aetiology



THE MALE GENITAL SYSTEM

All categories (B)
 7/13/22

CONGENITAL ANOMALIES (X)

1-PHIMOSIS:

Definition: This is congenital stenosis of the orifice of the prepuce.

Complications:

- Balanitis (inflammation of glans penis).
- Urinary tract obstruction (bilateral hydronephrosis).

2-CRYPTORCHIDISM:

Definition: This is failure of descent of one or both testis into the scrotum.

Aetiology:

- Short vas
- Hormonal disturbances
- Anomalies of testis, scrotum or inguinal canal.

Sites: The undescended testis may exist in abdomen, pelvis or inguinal canal

Complications: If untreated

- Testicular atrophy (infertility).
- Cryptorchidism is precancerous.

3-OTHER ANOMALIES as

- polyorchidism: supernumerary testis
- splenic- gonadal fusion

INFLAMMATORY DISEASES (X)

GONORRHEA (X)

Aetiology: It sexually transmitted gonococcal infection → suppurative inflammation of anterior urethra.

Pathology:

- Anterior urethritis characterized by purulent exudates. Microscopically dilated capillaries, oedema, neutrophils, pus cells & macrophages.
- Inguinal lymphadenitis may occur.

Complications:

- Direct spread of infection leading to cystitis, epididymo-orchitis, seminal vesiculitis. etc.
- Blood spread causing septicemia and acute infective endocarditis.
- Urethral stricture leading to urinary tract obstruction (bilateral hydronephrosis).

SPECIFIC INFECTIONS

- Tuberculosis
 - Bilharziasis
 - Syphilis
 - Filariasis
- For details see general pathology

NON-SPECIFIC INFECTIONS

BALANITIS: This is inflammation of glans penis caused by pyogenic bacteria as staphylococci, streptococci & gonococci. It is predisposed to by phimosis. It is precancerous.

PROSTATITIS:

1-Acute Prostatitis (Prostatic Abscess): Caused by pyogenic bacteria as staphylococci, gonococci ...etc. These bacteria reach the prostate directly from urethritis or cystitis, or by blood from distant infections. The prostate is enlarged, congested & infiltrated by neutrophils. Severe cases lead to abscess formation. The condition may change into chronic nonspecific cystitis.

2-Chronic Nonspecific Prostatitis: characterized by chronic inflammatory cell infiltrates (mostly lymphocytes). May follow acute prostatitis and may also accompany prostatic hyperplasia.

ORCHITIS & EPIDIDYMITIS

1-Acute Epididymo-Orchitis: Bacterial infection through direct spread (from cystitis, urethritis, etc) , lymphatic or blood spread. It is predisposed to by low immunity (as diabetics). It may lead to abscess formation. Healing by fibrosis may → epididymal obstruction (infertility may occur in bilateral cases)

2-Chronic nonspecific epididymitis and orchitis: May complicate the acute form.

3-Mumps Orchitis (Viral): It is a complication of mumps

4-Radiation Orchitis.

5-Idiopathic Granulomatous Orchitis: Granulomatous inflammation of unknown aetiology.

REMARK: Other types of epididymo-orchitis include:

1-Specific Infections: Bilharzial, Tuberculous, Syphilitic and Fungal infections (see general pathology)

2-Spermatic Granuloma of epididymis and vas. This is granulomatous inflammation occurring in the interstitial tissue around escaping sperms. The aetiology is unknown, but it is likely post-traumatic.

3-Malakooplakia of testis and epididymis.

NODULAR HYPERPLASIA OF PROSTATE (BPH) (BENIGN PROSTATIC HYPERTROPHY, SENILE PROSTATIC HYPERTROPHY)

At the age of 30 years, the prostate normally weighs 20 gm. Benign prostatic hypertrophy (BPH) affects 8% of men in their fourth decade, but the incidence rises to 50% in men in the fifth decade and 75% of men in the eighth decade.

PATHOGENESIS:

No predisposing or protecting factors (other than castration) have been identified. However recent studies relate BPH to an error in the metabolism of dihydrotestosterone.

* Site: middle & lateral loop near posterior loop

GROSS:

- 1-The weight of prostate in cases of BPH ranges between 35 g (mild cases) to 800 g or more. The average is around 100 g.
- 2-BPH affects the central and transitional zones of the prostate around the urethra. This part becomes enlarged and exhibits a nodular cut section. The urethra is compressed. The peripheral prostatic tissue is also compressed. The hyperplastic nodules may have a solid or spongy appearance.

MICROSCOPY:

- 1-Hyperplastic glands: The glands are enlarged with numerous cystic forms, acini are variable characteristically with a double epithelial lining showing infoldings. The lumens frequently contain inspissated glycoprotein material (corpora amylacea).
- 2-Hyperplastic fibromuscular stroma with lymphocytic infiltrates.
- 3-Prostatic infarcts are common in large prostates

EFFECTS AND COMPLICATIONS:

- 1-Compression of prostatic urethra leads to:
 - Difficult micturition.
 - Urine retention may occur.
 - Urinary incontinence may develop
- 2-Urinary tract obstruction →
 - Bladder hypertrophy, dilatation and diverticula.
 - Bilateral hydronephrosis and hydronephrosis → renal failure.
- 3-Urinary stasis due to obstruction → infection (cystitis, pyelonephritis... etc) → stone formation.

What is corpora amylacea
it's inspissated glycoprotein material in lumen of hyperplastic enlarged prostatic glands

* Not pre Cancerous bec. arise from middle & lateral loop = Central + Transitional

CARCINOMA OF THE PROSTATE

Cancer prostate is extremely common. The incidence rises steadily with age. Most cases occur after the age of 50 years. Most cases are hormone dependant (androgens), therefore carcinoma does not occur in persons castrated before puberty.

PREMALIGNANT LESIONS OF THE PROSTATE

- 1-Prostatic intraepithelial neoplasia (PIN) was the accepted term for premalignant prostatic lesions. PIN is characterized by hyperplastic glands showing cellular atypia in the form of cellular stratification, nuclear enlargement and nucleolar prominence.
- 2-Atypical adenomatous hyperplasia (AAH)

PATHOLOGICAL FEATURES:

Serum markers of prostatic cancer.

- 1-Prostatic specific antigen (PSA) is very useful marker for the diagnosis and follow up of prostatic adenocarcinoma (Normal serum value: 0-4). It is elevated in cases of prostatic cancer.
- 2-Acid phosphatase is also secreted by tumor cells and is another useful marker.

Gross: Most carcinomas of the prostate arise from the peripheral zone, rarely carcinoma arises from the transitional periurethral zone. Cancer prostate vary in size and present as a hard poorly defined yellowish nodule or multifocal nodules (80% multifocal).

Microscopy: The commonest pattern is prostatic adenocarcinoma. It may be well differentiated, moderately differentiated or poorly differentiated. This grading was modified by Gleason (1977) & this is till now the most accepted method of microscopic grading of prostatic adenocarcinoma.

- Gleason described five grades of prostatic adenocarcinoma:

- 1-Gleason grade 1: Closely packed uniform acini lined by a single cell layer.
- 2-Gleason grade 2: Small separate less uniform acini, lined by a single cell layer
- 3-Gleason grade 3: Cribriform or papillary pattern.
- 4-Gleason grade 4: Infiltrative fused glands with solitary cells or clear cells
- 5-Gleason grade 5: Solid sheets, strands or focal tumoral necrosis (comedo pattern).

- A final Gleason score; is made by adding the numerical values of the two most predominant grades (e.g Gleason grades 1+3 = score 4). Gleason scoring system is interpreted as follows:

- 1-Low-grade (well differentiated) carcinoma correspond to Gleason score 2-4
- 2-Medium grade (moderately differentiated) correspond to Gleason score 5-7
- 3-High grade (poorly differentiated) carcinoma correspond to Gleason score 8-10

SPREAD:

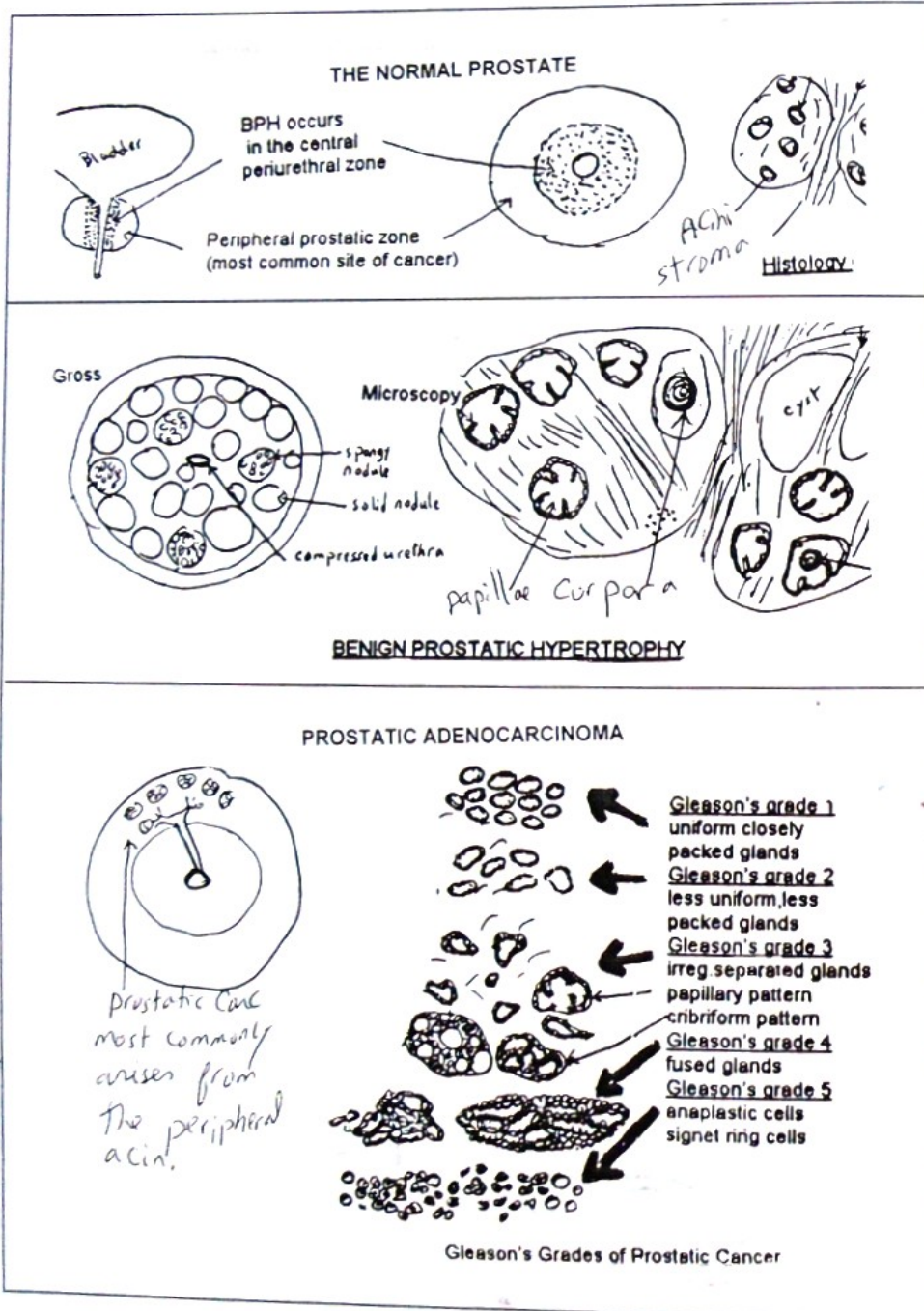
- Direct spread:** leads to invasion of prostatic capsule, prostatic urethra, bladder and rectum. Perineural spread is common.
- Lymphatic spread:** to pelvic & retroperitoneal lymph nodes, then to supra-diaphragmatic nodes.
- Blood spread:** to bone (osteoblastic metastases), lungs, skin, brain, penis, liver & adrenal glands.

STAGING OF PROSTATIC CARCINOMA:

- T1: Clinically unapparent, tiny tumor.
- T2: Tumor confined within the prostate
- T3: Capsular infiltration or invasion of seminal vesicles.
- T4: Infiltration to levator muscle or fixed to pelvic wall.

* Complication: Painful
* H/DH: Haemorrhage
2° infection
Disturbance of function
+ Loss of function

Remember: Cancer prostate is Painful
Paralytic
Bone
Pain
Pain



TUMORS OF TESTIS

CLASSIFICATION OF TESTICULAR TUMORS ACCORDING TO ORIGIN

- 1-Germ Cell Tumors:** Malignant
 - a) Seminoma & spermatocytic seminoma
 - b) Teratomas, embryonal carcinoma, teratocarcinoma, choriocarcinoma
 - c) Yolk sac tumor
- 2-Sex Cord-Stromal Tumors:** Benign or malignant
 - a) Leydig cell (interstitial cell) tumor
 - b) Sertoli cell tumor (androblastoma)
 - c) Granulosa cell tumor
 - d) Mixed types, Sertoli-Leydig cell tumor
- 3-Mixed Germ Cell-Sex Cord Stromal Cell Tumors (Gonadoblastoma)**
- 4-Tumors of Rete Testis:** a) Adenoma, cystadenoma, adenofibroma b) Carcinoma
- 5-Lymphoma.**
- 6-Paratesticular Tumors (tumors of epididymis, tunica vaginalis and soft tissue) as:**
 - a) Adenomatoid tumor
 - b) Neurofibroma, leiomyoma, lipoma
 - c) Mesothelioma
 - d) Epididymal cystadenoma & carcinoma
 - e) Rhabdomyosarcoma
 - f) Vascular tumors
 - g) Others
- 7-Secondary Tumors (metastases).**

I-BENIGN TUMORS (B)

1-LEYDIG CELL TUMOR (interstitial cell tumor):

- A rare benign tumor.
- Gross: It appears as a rounded yellowish mass
- Microscopy: It consists of proliferated Leydig cells.
- The tumor cells secrete androgens & oestrogens. In children it may → precocious puberty

2-SERTOLI CELL TUMOR: A rare benign tumor secreting oestrogens.

3-OTHERS as:

- a) Mature teratoma
- b) Benign paratesticular tumors as epididymal adenoma, neurofibroma, leiomyoma, lipoma, angioma & others.

II-MALIGNANT TUMORS

SEMINOMA (40%)

Definition & Origin: It is a malignant tumor arising from germ cells (seminiferous) of the testis. It is the commonest testicular tumor (40%) & has a better prognosis, since it is radiosensitive.

Gross: The testis is moderately enlarged. Cut section shows a noncapsulated solid homogenous pale yellow growth, sometimes with small necrotic foci.

Microscopy: Many types:

1-Classic Seminoma: It consists of uniform large cells with abundant clear cytoplasm and large central nuclei containing large nucleoli. The cells exist in groups separated by fibrous bands invariably infiltrated by lymphocytes and plasma cells.

2-Spermatocytic seminoma: It consists of cells showing marked size variations (a mixture of small cells, large cells & bizarre giant cells). Mitoses may be numerous and lymphocytic infiltration is absent.

3-Other types such as Classic seminoma with trophoblastic giant cells & anaplastic seminoma (seminoma with high mitotic activity).

Age: Spermatocytic seminoma occurs in old age groups (around 65 years). Other types of seminoma occur around the age of 30-40 years.

Spread of Seminoma (& other malignant testicular tumors).

- 1-Direct: to testicular adnexa and scrotal wall.
- 2-Lymphatic: Para-aortic lymph nodes.
- 3-Blood: Lung, liver, brain, and bone.

Metastasis: Seminoma → seminoma + lymphoepithelioma
Benign = Adeno lymphoma has benign lympho

Seminoma ♂
= Dysgermenoma ♀

Oral Germ cell tumors
♂ vs. ♀

VIP
A
Cyst
cells
2011

V.V. rare
oral + Hc Q

undifferentiated

U 65-5

A + VIP + Case
Jar + slide + cyst
2011

Aetiology = testis + over heat
→ + infertility

White Knight

Prognosis: Seminomas are radiosensitive tumors.

1-Spermatocytic seminoma never metastasizes and has an excellent prognosis.

2-Classic seminomas stage I (limited to testis) or stage II (spread to intra diaphragmatic lymph nodes) have also excellent prognosis and over 95% of these patients are cured. With stage III (metastases), the prognosis is unfavorable.

* arise from totipotent germ cell

TERATOMA GROUP (32%)

1-Mature (differentiated) teratoma:

- A benign tumor that may undergo malignant transformation.
- It consists of a mixture of mature tissues derived from ectoderm, endoderm & mesoderm.
- It grossly appears as a rounded tumour, usually with multiple cysts.

2-Immature teratoma:

- This is a malignant tumor which grossly shows necrosis & hemorrhage.
- Microscopically it consists of a mixture of tissues derived from ectoderm, endoderm & mesoderm; some of which appear immature (malignant), whether epithelial, mesenchymal or both.

3-Other tumors which are sometimes classified among the teratoma group:

- **Embryonal carcinoma:** Sometimes considered undifferentiated teratoma. It consists of very primitive cells with high anaplasia & frequent mitosis.
- **Teratocarcinoma:** A mixture of embryonal carcinoma & classic teratoma.
- **Choriocarcinoma:** It is a highly malignant tumor which consists of malignant trophoblastic epithelium (placental type tissue). It is sometimes considered as a monodermal teratoma. It secretes human chorionic gonadotropin.
- **Carcinoid tumor:** similar to that of GIT. It is sometimes considered a monodermal teratoma.

YOLK SAC TUMOR (Endodermal sinus Tumor)

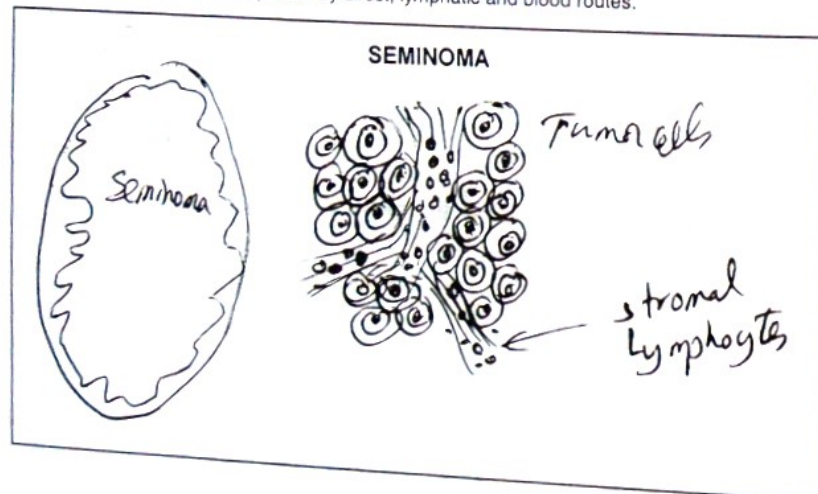
It mostly occurs in infants. It consists of very primitive cells exhibiting microcystic, glomeruloid, hepatoid, clear cell and papillary structures (resembling the normal yolk sac).

TUMORS OF THE PENIS (X)

1-BENIGN as Squamous cell papilloma

2-MALIGNANT as Squamous cell carcinoma:

It is a rare tumor predisposed to by balanitis which is more common in uncircumcised people. It spreads by direct, lymphatic and blood routes.



HYDROCELE

Definition: Accumulation of serous fluid in the tunica vaginalis sac.

Aetiology:

- 1-Primary (idiopathic) type: This is the most common type. Undetermined aetiology.
- 2-Congenital: Patent processus vaginalis.
- 3-Acquired:
 - a) Inflammations of epididymis & testis & filariasis of spermatic cord.
 - b) Tumors of epididymis & testis
 - c) Trauma and torsion of testis.

Effects: Tunica shows fibrous thickening. Some cases may be complicated by:

- 1-Testicular atrophy in prolonged cases.
- 2-Secondary infection.

VARICOCELE

Definition: Varicosity (elongation, dilatation & tortuosity) of the pampiniform venous plexus.

Types:

- 1-Primary (idiopathic, non-obstructive) type: Common in young males, particularly in the left side. It may be to marked congestion caused by unrelieved sexual excitement
- 2-Secondary type due to a) chronic general venous congestion b) obstruction of spermatic veins (e.g left varicocele in case of left renal cell carcinoma).

Effects: Hypospermatogenesis may occur leading to infertility.

HEMATOCELE (X)

Definition: Blood accumulating in the tunica vaginalis sac

Aetiology:

- 1-Local causes as trauma or tumors.
- 2-General causes of bleeding as leukemia

Effects:

- 1-Fibrosis, calcification and pressure atrophy of the testis.
- 2-Secondary infection (pyocele).

CHYLOCELE (X)

Chylous effusion within the tunica vaginalis sac is caused by lymphatic obstruction (e.g filariasis)

INFERTILITY (X)

The causes of male infertility include:

1-PRETESTICULAR CAUSES: Hormonal abnormalities.

2-TESTICULAR CAUSES (most common aetiology of infertility) **The common patterns are:**

- a) **Maturation Arrest:** Spermatogenesis is arrested at the phase of spermatocytes (or rarely spermatids). No sperms are produced (azoospermia).
- b) **Germ cell aplasia (Sertoli Cell Only Syndrome):** Azoospermia is due to aplasia of germ cells.
- c) **Klinefelter's Syndrome:** Azoospermia is due to chromosomal abnormality (XXY).
- d) **Hypospermatogenesis:** This is reduction of all germ cell phases. Sperm formation occurs but in reduced numbers. Varicocele is sometimes associated with hypospermatogenesis.
- e) **Bilateral orchitis.**

3-POST-TESTICULAR CAUSES (OBSTRUCTIVE AZOOSPERMIA): Spermatogenesis is present, but the sperm pathway is obstructed due to congenital, idiopathic or post inflammatory strictures of the vas deferens.

DISEASES OF THE FEMALE GENITAL SYSTEM

DISEASES OF THE CERVIX

CERVICITIS

DEFINITION & AETIOLOGY:

- Inflammation of cervix (mainly endocervix) is extremely common.
- It may be sexually transmitted e.g. gonorrhea.
- It is more commonly caused by Staphylococci or Streptococci following labour due to cervical lacerations.

TYPES: Cervicitis may be:

- 1-Acute cervicitis characterized by swollen congested cervix associated with purulent discharge.
- 2-Chronic cervicitis.

PATHOLOGY of chronic cervicitis:

- 1-Cervical Erosion: This is a red patch on the external os that bleeds easily on touch.

It is due to acute inflammation of the external os manifested by necrosis and shedding of the stratified epithelium of the external os as well as hyperemia of the subepithelial tissue.

The columnar cells of the endocervix creep and cover the bare external os. These cells are less resistant than the original stratified epithelium producing bleeding on touch.

- 2-Nabothian Follicles: When inflammation involves the endocervical glands they become distended with exudate leading to multiple small cysts (Nabothian follicles = retention cysts).

- 3-Squamous Metaplasia of the endocervical mucosa occurs in chronic cases. It may be associated with dysplasia (cervical intraepithelial neoplasia = CIN) which is precancerous.

- 4-Polypoid Endocervicitis (cervical polyp): Inflammatory cervical polyps may develop in chronic cases.

- Gross: May be sessile or pedunculated soft pink polyp that easily bleeds on touch.

- Microscopy: The polyp is covered by columnar or metaplastic stratified squamous epithelium. The polyp core shows chronic inflammatory cells, fibrosis and proliferated endocervical glands.

- 5-Ectropion: This is eversion of cervical lips due to marked fibrosis.
- 6-Persistent discharge (leucorrhea).

COMPLICATIONS:

- 1-Contact bleeding (during sexual intercourse).
- 2-Ectropion may lead to habitual abortion.
- 3-Spread of infection may lead to endometritis, salpingitis.
- 4-Carcinoma on top of squamous metaplasia and dysplasia (CIN).

GONORRHEA (X)

Definition & Aetiology: A sexually transmitted gonococcal infection

Pathology & Complications:

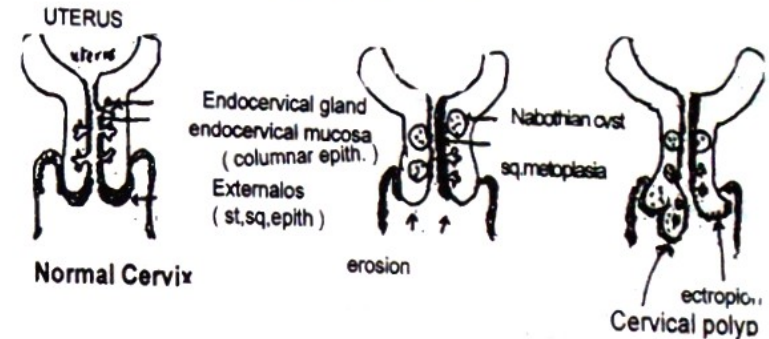
- 1-Urethritis: Mucosa appears hyperemic & covered by purulent exudates. Microscopically it shows dilated capillaries, neutrophils and pus cells. Healing occurs but fibrous stricture is rare.
- 2-Paraurethritis this is inflammation of paraurethral glands.
- 3-Bartholin's gland inflammation: This may lead to abscess (Bartholin's abscess). Obstruction of the gland ducts lead to cyst formation (Bartholin's cyst).

- 3-Cervicitis leading to cervical erosion (describe), Nabothian follicles (describe), squamous metaplasia (describe) or polypoid endocervicitis (describe).
- 4-Vaginitis and endometritis are rare.

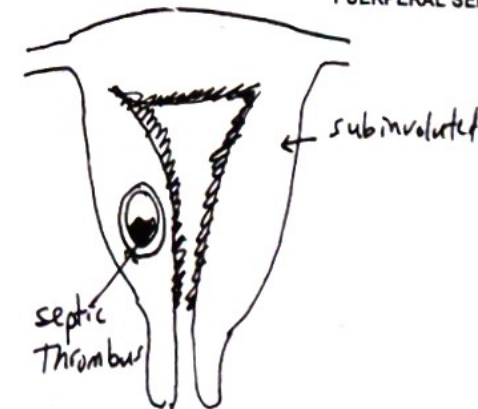
- 5-Salpingitis. This may be associated with one of the following:

- a-Hydrosalpinx (tubal distension with serous exudate).
- b-Pyosalpinx (tubal distension with pus).
- c-Mucocele (tubal distension with mucus).
- d-Tubo-ovarian abscess (salpingo-oophoritis).
- e-Pelvic inflammatory disease (pelvic peritonitis).
- f-Tubal fibrosis and obstruction leading to ectopic tubal pregnancy or to sterility.

CHRONIC CERVICITIS



PUERPERAL SEPSIS



TUMORS OF THE CERVIX & UTERINE BODY

BENIGN TUMORS:

1- Cervix:

- a) Squamous cell papilloma (Condyloma)
- b) leiomyoma
- c) Cervical polyp

2- Uterine Body:

- a) Leiomyoma
- b) Endometrial polyp

MALIGNANT TUMORS:

1- Cervix

- a) Carcinoma
- b) leiomyosarcoma
- c) Sarcoma botryoides

2- Uterine Body:

- a) Carcinoma
- b) leiomyosarcoma
- c) Endometrial stromal sarcoma
- e) Mixed mesodermal (Mullerian) tumors.

CARCINOMA OF THE CERVIX

PREDISPOSING FACTORS:

- 1- Females with early age of first intercourse.
- 2- Females with multiple sexual partners. Cancer cervix is more common in prostitutes & rare in virgins
- 3- Multiparous females.
- 4- High risk male sexual partners (particularly uncircumcised men).
- 5- Human papilloma virus infection, particularly type 16 & 18 (sexually transmitted).
- 6- Chronic cervicitis.
- 7- Cervical dysplasia (cervical intraepithelial neoplasia or CIN): see below.

Origin: 1) Squamous epithelium (ectocervical or metaplastic endocervical) → squamous cell carcinoma 2) Less commonly endocervical glandular epithelium → adenocarcinoma

PATHOLOGY:

- 1-CERVICAL INTRAEPITHELIAL NEOPLASIA (CIN):** These are non-neoplastic precancerous lesions. Grossly may appear as a small indurated patch. Microscopically there is cellular atypia & loss of polarity with no basement membrane invasion. There are 3 grades of CIN:
- a) CIN-I (mild dysplasia): Atypia involves the lower 1/3 of cervical mucosa. May regress.
 - b) CIN-II (moderate dysplasia): cellular atypia affecting the lower 2/3 of cervical mucosa
 - c) CIN-III (severe dysplasia or carcinoma in situ): diffuse cellular atypia affecting the whole thickness of cervical mucosa. Some of these cases (about 30%) → invasive carcinoma.

2-INVASIVE CARCINOMA:

Gross: The tumor starts as a small indurated nodule, as it grows it takes one of two patterns:

- a) Exophytic carcinoma (protrude into vagina): Verrucous mass or polypoid fungating mass.
- b) Endophytic carcinoma (deeply invading): Nodular infiltrative growth or ulcerative growth.

Microscopy:

- a) Squamous cell carcinoma (90%): nonkeratinizing and keratinizing types.
- b) Adenocarcinoma (5%) from endocervical mucosa.
- c) Adenosquamous carcinoma (rare).
- d) Undifferentiated carcinoma.

Spread:

1-Direct:

- a) Downwards to upper vagina.
- b) Upwards producing obstruction of cervical canal.
- c) Anterior to bladder and ureters.
- d) Posterior to rectum.

Effects of direct spread:

- Renal failure due to ureteric obstruction.
- Fistulae with bladder or rectum.
- Pyometria: Pus filling the uterus due to secondary infection in the presence of cervical obstruction.

2-Lymphatic to pelvic lymph nodes.

3-Blood Late to lungs, liver, bones.

Staging Of Cervical Cancer:

Stage 0: Carcinoma in situ.

Stage I: Carcinoma confined to cervix.

Stage II: Carcinoma extending to upper vagina.

Stage III: Carcinoma extending to pelvic wall.

Stage IV: Carcinoma extending to nearby organs (bladder, rectum) or distant spread.

Prognosis: Exophytic is better than endophytic types.

Death is due to metastases, uremia, toxemia or Hge.

EMBRYONAL RHABDOMYOSARCOMA (SARCOMA BOTRYOIDES)

The tumor mainly occurs in infants and children.

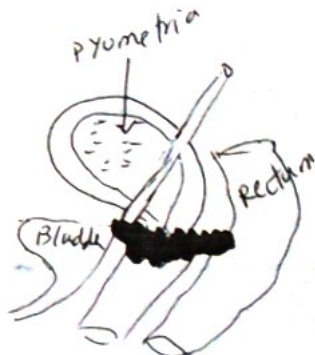
The most common sites are the **vagina and cervix**.

Grossly it appears as a polypoid soft edematous mass resembling a bunch of grapes.

Microscopically, it consists of a loose myxoid stroma containing a variable mixture of small neoplastic cells and larger somewhat differentiated cells with cross striations (rhabdomyoblasts).

Prognosis: Recent chemotherapy protocols have considerably improved the prognosis.

CARCINOMA OF CERVIX



Cancer Cervix
invading bladder
& rectum
(advanced stage)

DISEASES OF THE UTERINE BODY

THE MENSTRUAL CYCLE

THE NORMAL MENSTRUAL CYCLE (average 28 days) consists of:

1-Menstruation: First 3 days (average).

2-Follicular (proliferative) phase: Day 4-14 of the cycle.

- It is under the influence of oestrogen produced by the graffian follicles.
- The endometrial glands are tubular and are lined by cubical epithelium. The stroma is cellular.

3-Ovulation: At day 14/15.

4-Luteal (secretory) phase: day 16-28 of the cycle.

- It is under the influence of progesterone produced by the corpus luteum corpus luteum.
- First the glands show subnuclear secretory vacuoles, then supranuclear vacuoles. The enlarge and acquire a tortuous "cork-screw" appearance. The stroma is first oedematous then glands becomes decidualized.
- 5-Menstruation:** Occurs if the ovum is not fertilized, since in these cases the corpus luteum regresses (corpus albicans) leading to withdrawal of hormones which produce shedding of the endometrium and bleeding. Only the basal layer of endometrium is left.

CAUSES OF ABNORMAL UTERINE BLEEDING

Abnormal uterine bleeding (menorrhagia or metrorrhagia) may be due to:

1-DYSFUNCTIONAL UTERINE BLEEDING (DUB): This is bleeding caused by hormonal dysfunction without an organic cause as in cases of:

a)Anovulatory causes: These lead to bleeding (as well as infertility):

- Exaggerated-disordered proliferative endometrium due to unopposed action of oestrogen.
- Endometrial hyperplasia (the extreme form of disordered proliferation)
- Endometrial atrophy

b)Ovulatory luteal phase defects:

- Persistent corpus luteum → prolonged luteal phase → irregular shedding of endometrium
- Inadequate or retarded luteal phase: It leads to bleeding and may cause infertility.
- Irregular hormone response: It leads to bleeding and may cause infertility.

2)LOCAL ORGANIC CAUSES:

- Disorders of pregnancy as abortion, tubal pregnancy and placental tumors.
- Benign tumors as leiomyoma, endometrial polyp.
- Malignant tumors as carcinoma of cervix or uterus and sarcomas.
- Inflammations as cervicitis (cervical erosion) and endometritis.
- Adenomyosis.

3)GENERAL CAUSES OF BLEEDING as hypertension, leukemia, purpura...etc.

ENDOMETRIAL HYPERPLASIA

It is a common condition, most commonly developing around menopause.

Aetiology: it is a common condition caused by prolonged oestrogen stimulation due to:

- Repeated anovulatory cycles (common at premenopause)
- Oestrogen secreting tumors (granulosa cell and/or theca cell tumors).
- Prolonged oestrogen therapy.
- Others as polycystic disease of ovary and adrenal hyperfunction.

Gross: Mildly enlarged uterus with thick polypoid endometrium.

Microscopy: The stroma and glands are hyperplastic. Glandular hyperplasia may be:

- Simple hyperplasia (cystic hyperplasia):** it is characterized by crowded glands with numerous cystic forms (giving a Swiss-cheese appearance). The glands are lined by columnar cells showing no atypia. It has a low precancerous potential.

Swiss cheese = Cystic hyperplasia

endometrial hyperplasia = CIN 1

2-Complex hyperplasia (adenomatous hyperplasia): it is characterized by crowded back to back glands lined by columnar epithelium. It is considered as an intermediate grade hyperplasia that may (in less than 5% of cases) progress to adenocarcinoma.

3-Atypical hyperplasia (complex hyperplasia with atypia): this is adenomatous hyperplasia accompanied by cell atypia such as loss of polarity, hyperchromatism and nucleolar prominence. The risk of cancer development is higher than with other types of endometrial hyperplasia and correlates with the degree of atypia. (most commonly p (e) can follow)

Complications:

1-Abnormal uterine bleeding (also known as dysfunctional uterine bleeding). It may be:

- menorrhagia (excessive prolonged menstruation).
- metrorrhagia (irregular bleeding).

2-Malignancy: most commonly on top of atypical hyperplasia.

ENDOMETRITIS

Definition & types: This is inflammation of endometrium. It is uncommon. Types include

- Acute as: a) puerperal sepsis b) gonococcal endometritis c) chlamydial endometritis

2-Chronic as:

- infections associated with intrauterine contraceptive devices
- tuberculous endometritis
- Bilharzial endometritis.

PUERPERAL SEPSIS

Definition: This is infection of the uterus (endometrium mainly), following labour or abortion.

Aetiology:

- Predisposing factors:** 1) Retained clots or placental fragments. 2) Low resistance.
- Causative bacteria:** Pyogenic bacteria, most commonly Streptococcus hemolyticus, less commonly E coli and others
- Route of infection:** Bacteria reach the uterus through:
 - Endogenous route: Direct (from vulva or vagina), or hematogenous (from distant infection).
 - Exogenous route (from outside the patient) e.g. contaminated gloves or instruments.

Gross:

- The uterus is subinvolved (large) and soft.
- The endometrium shows a yellow purulent exudate.
- The myometrial veins may show septic thrombi (septic thrombophlebitis).

Microscopy:

- The endometrium shows septic endometritis (necrosis, neutrophils, pus cells, dilated capillaries).
- In severe cases the myometrium shows septic myometritis (myometrial abscesses).

Complications:

- Severe toxemia leading to toxic myocarditis and other toxic effects.
- Septic thrombophlebitis leading to pyemia.
- Septicemia.
- Direct spread leading to septic peritonitis, parametritis, salpingitis or salpingo-oophoritis.
- Infertility.

ADENOMYOSIS

Definition: This is the presence of endometrial foci inside the myometrium.

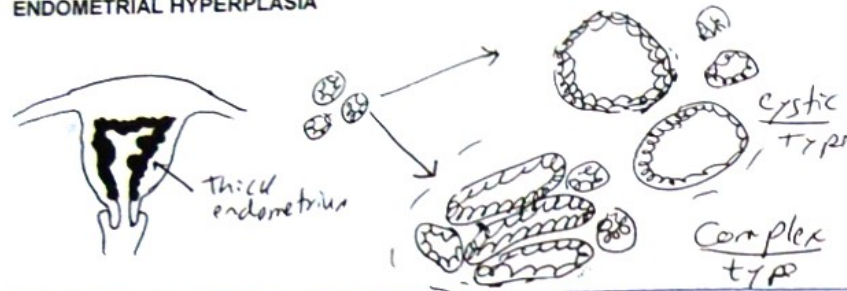
Pathogenesis: These foci are likely derived from the basal layer of the endometrium.

Pathological Features:

- Gross:** enlarged uterus. thick myometrium showing small grayish or hemorrhagic foci.
- Microscopy:** the myometrium shows foci composed of endometrial glands and stroma (adenomyosis) or sometimes endometrial stroma only (stromal endometriosis).
- Complications:**
 - Menorrhagia.
 - Dysmenorrhoea (painful menstruation).

Adenomyosis = gland (endometrial) in muscle (myometrium)

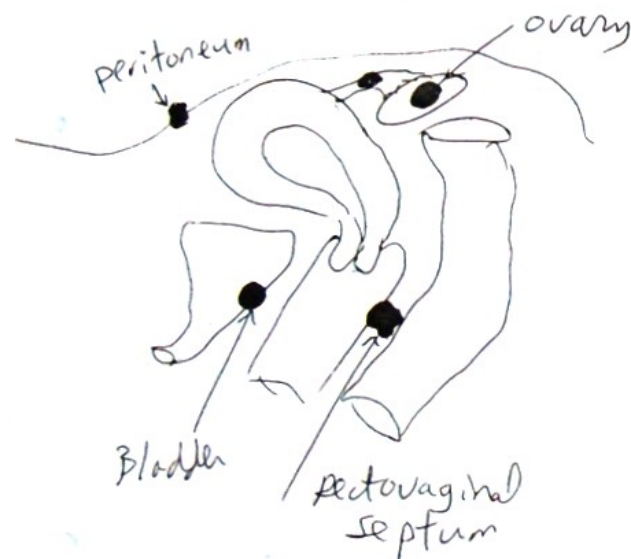
ENDOMETRIAL HYPERPLASIA



ADENOMYOSIS



ENDOMETRIOSIS



ENDOMETRIOSIS

Definition: This is the presence of endometrial tissue outside the uterine wall.

Sites:

1-Genital:

- Ovaries.
- Fallopian tubes.

2-Extragenital:

- Wall of urinary bladder or intestine.
- Rectovaginal septum.
- Pelvic peritoneum.
- Umbilicus.
- Lungs, lymph nodes...

Pathogenesis: Unknown.

- 3 theories
- Ovarian, tubal and pelvic peritoneal endometriosis may be due to regurgitation (reflux) of shed menstrual endometrial glands, which become implanted in these sites.
 - It may be due to metaplasia of serosal cells covering the ovary, rectum...
 - It may be due to lymphatic or vascular emboli of endometrial tissue.

Complications: Pain and hemorrhage in the affected area. The ovaries show chocolate cyst. Peritoneal hemorrhage may be followed by fibrosis and adhesions.

TUMORS OF THE UTERINE BODY LEIOMYOMA

Origin:

It is the commonest tumor of adult females (affecting 25% of females above the age of 25 years), arising from the uterine smooth muscle.

Gross Picture:

- Single or multiple.
- Occurs within the myometrium (intramural, interstitial), but may also occur beneath the serosa (subserous) or immediately beneath the endometrium (submucous).
- Sharply circumscribed, round and firm.
- Uncapsulated. May acquire false capsule of compressed surrounding muscles.
- The cut section is greyish or greyish brown and usually shows a whorly appearance.

Microscopic Picture:

- Interlacing bundles of smooth muscle cells, which are spindle shaped cells that differ from fibroblasts in having more abundant eosinophilic cytoplasm and rod-shaped nuclei having blunt (non-tapering) ends.
- Fibrous stroma containing blood vessels. This fibrous stroma may be abundant (particularly after the menopause) and the tumor may then be called fibromyoma or fibroid.
- Secondary changes are common (except malignant change) and include:
 - Hyaline degeneration.
 - Myxomatous degeneration.
 - Cystic changes: due to myxomatous degeneration.
 - Ischemic necrosis (red degeneration) which is common during pregnancy due to vascular thrombosis. The tumor appears red and necrotic.
 - Ulceration of endometrium & secondary infection
 - Dystrophic calcification
 - Malignant transformation into leiomyosarcoma is extremely rare.

Complications:

- Uterine bleeding
- Infertility.
- Malignant change (very rare if ever)

ENDOMETRIAL POLYP

A common benign tumor.

Gross: Single or multiple, sessile or pedunculated, greyish polyp.

Microscopy: a) Proliferated variable sized endometrial glands b) Fibrous stroma c) Thick walled vessels.

Complications: Abnormal uterine bleeding is the main complication.

ENDOMETRIAL CARCINOMA

The tumor is uncommon. It mainly occurs after menopause. Predisposing factors include nulliparity and endometrial hyperplasia (particularly the atypical type).

Gross: Common in fundus; uterus is enlarged. The tumor may be:

- 1- Erupting polypoid mass.
- 2- Diffuse infiltrating carcinoma.

Microscopy:

1- Adenocarcinoma or papillary adenocarcinoma: Commonest.

2- Adenoacanthoma: This is adenocarcinoma in which some malignant glands show squamous metaplasia.

3- Adenosquamous carcinoma: A mixture of adenocarcinoma and squamous carcinoma.

Spread:

- 1- Direct to fallopian tubes, cervix, bladder, rectum....
- 2- Lymphatic to pelvic lymph nodes.
- 3- Blood: Late to lungs, liver, bone...

ENDOMETRIAL SARCOMAS (X)

1- **Leiomyosarcoma:** See general pathology

2- **Endometrial stromal sarcoma:** A rare spindle cell sarcoma arising from endometrial stroma.

3- **Mixed Mesodermal Tumors:** a) **Mullerian Adenosarcoma** It is a sarcoma mixed with benign glandular structures b) **Malignant Mixed Mullerian Tumor (carcinosarcoma):** It is a highly malignant tumor arising in elderly women as a large polypoid fleshy mass that microscopically consists of a mixture of adenocarcinoma and sarcomatous elements.

UTERINE BODY TUMORS



Leiomyoma



Endometrial Carcinoma



Endometrial Polyp

What is Adenoacanthoma?

DISEASES OF THE OVARIES

TUMORS OF THE OVARY

I-SURFACE EPITHELIAL TUMORS

The surface epithelium of the ovary can differentiate along different pathways giving rise to different tumors; which may be tubal epithelial differentiation (serous tumors), endocervical epithelial differentiation (mucinous tumors), endometrial epithelial differentiation (endometrioid tumors) or rarely transitional epithelial differentiation (Brenner tumors). Each may be benign, borderline or malignant.

a) **Serous tumors:** Benign (cystadenoma), malignant (carcinoma) or intermediate (borderline malignancy).

b) **Mucinous tumors:** Benign, malignant or intermediate (borderline malignancy).

c) **Endometrioid tumors:** Benign, malignant or intermediate (borderline malignancy).

d) **Brenner tumors:** Benign, malignant or intermediate (borderline malignancy).

e) Clear cell carcinoma (rare)

A) BENIGN SURFACE EPITHELIAL TUMORS:

1- MUCINOUS CYSTADENOMA

* GROSS FEATURES

- Usually unilateral and pedunculated.
- May assume a huge size.
- Multilocular. The locules have a smooth lining and contain bluish mucinous material.

2- SEROUS CYSTADENOMA

* GROSS FEATURES

- Usually bilateral. May be pedunculated.
- Small to moderate in size (up to 30 cm).
- Usually unilocular. The locules have a smooth lining & contain clear serous fluid. The lining may show papillary projections & in these cases the tumor is termed **Serous Papillary Cystadenoma**.

MICROSCOPY

Cysts are lined by columnar mucin secreting cells. The lining is cubical cells.

COMPLICATIONS

- 1- Torsion of the pedicle leading to: a) Ascites. b) Hemorrhage. c) Shock.
- 2- Pressure effects on bladder, rectum.
- 3- Malignant change (cystadenocarcinoma) is more common with papillary types.
- 4- Rupture of mucinous cystadenoma producing pseudomyxoma peritonei.
- 5- Secondary infection.

3- BENIGN BRENNER TUMOR:

A rare tumor. Grossly appears as a solid capsulated mass. Microscopically consists of nests of transitional cells embedded in fibrous stroma.

4- **BENIGN ENDOMETRIOID TUMOR:** Rare tumor. Most endometrioid tumors are malignant.

B) SURFACE EPITHELIAL TUMORS OF BORDERLINE MALIGNANCY:

Any of the surface epithelial tumors may be categorized as border line malignancy. The most common of these are the serous & mucinous types, they are characterized by cytoarchitectural atypia in the form of more complex papillary formations, cellular stratification with disturbed polarity and nuclear atypia; unaccompanied by stromal invasion.

C) MALIGNANT SURFACE EPITHELIAL TUMORS: OVARIAN CARCINOMA

Origin: The tumor arises de novo or as a malignant transformation in a pre-existing benign tumor.

Gross: The tumor may be unilateral or bilateral, solid or partially cystic, sometimes with gelatinous areas (in case of mucinous cystadenocarcinoma). Areas of necrosis and hemorrhage are present. Hemorrhagic ascites is common when peritoneum is invaded.

IV- OTHER OVARIAN TUMORS

A) FIBROMA:

May occur as a part of Meig's syndrome (ovarian fibroma, ascites and hydrothorax).

B) LYMPHOMA: Rare.

C) **METASTATIC TUMORS:** The ovaries are common sites of metastases.

Krukenberg tumors: These are bilateral metastatic tumors composed of mucin secreting cells (signet ring cells). The primary is usually a gastric carcinoma. The tumors can also occur with any primary mucin secreting carcinoma (colon, pancreas, gall bladder, breast, etc).

OVARIAN CYSTS

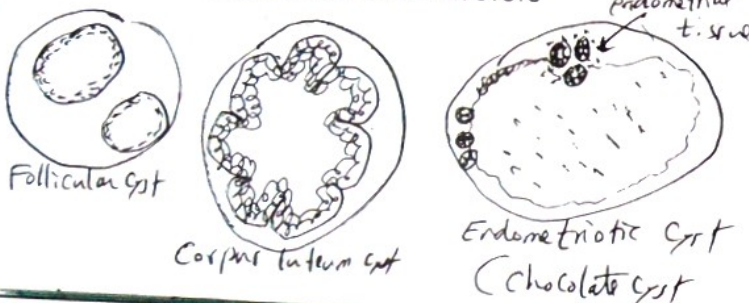
NEOPLASTIC CYSTS:

- 1-Cystic teratoma (dermoid cyst)
- 2-Cystadenomas.
- 3-Cystadenocarcinoma.

NON-NEOPLASTIC CYSTS:

- 1-Follicular Cysts: Multiple small cysts arising from non-rupturing graffian follicles They are lined by granulosa cells and contain clear fluid.
- 2-Stein-Leventhal syndrome: Polycystic ovaries showing multiple follicular cysts, associated with hirsutism, oligomenorrhea and infertility.
- 3-Corpus Luteum Cyst: A single large cyst arising from corpus luteum of menstruation or pregnancy. Intracystic hemorrhage is common.
- 4-Chocolate Cysts: Hemorrhagic cysts in case of ovarian endometriosis.
- 5-Theca Lutein Cysts: Multiple cysts lined by luteinizing theca cells occurring in cases of placental tumors

NON-NEOPLASTIC OVARIAN CYSTS



DISEASES OF THE PLACENTA

Placental diseases: 1) congenital anomalies 2) infections 3) tumors (gestational trophoblastic disease).

GESTATIONAL TROPHOBLASTIC DISEASE

This is a group of placental disorders (tumors) characterized by benign or malignant trophoblastic proliferation. This group includes:

- 1-Hydatidiform mole (vesicular mole): a) Complete mole. b) Partial mole. c) Invasive mole.
- 2-Choriocarcinoma.
- 3-Placental site trophoblastic tumor.

Complete mole
Partial mole
Placenta
VIP
155
Jaw + slide
Common Benign Tumour of placenta
VIP + 500 + A + Case 2011
Hassa

VESICULAR (HYDATIDIFORM) MOLE

1-COMPLETE MOLE

- All chorionic villi are transformed into vesicles.
- No fetus.
- Complete mole is thought to be due to abnormal fertilization e.g. fertilization of an "empty" ovum with 2 sperms.
- Chromosomal number is diploid (normal) i.e. 46 XX or 46 XY.

GROSS:

- 1-Uterus is disproportionately large for the age of gestation.
- 2-The placenta appears as a large mass composed of vesicles, 1-30 mm each; giving the appearance of a bunch of grapes.
- 3-The ovaries show theca lutein cysts.

MICROSCOPY:

- 1-Marked trophoblastic proliferation.
- 2-Hydropsic oedematous cores showing no vessels.

SERUM CHORIONIC GONADOTROPIN

is high (positive pregnancy test). +++++

COMPLICATIONS:

- 1-Transformation into invasive mole or choriocarcinoma is not uncommon.
- 2-Massive uterine bleeding may occur.

2-PARTIAL MOLE

- There is a mixture of vesicles and normal villi.
- Fetus may be anomalous, but often present.
- Partial moles are thought to be related to fetal anomalies and death (blighted ovum).
- Chromosomal number is often triploid i.e. 69 XXX or 69 XXY.

GROSS:

- 1-Uterine size is proportionate for the age of gestation.
- 2-The placenta appears slightly enlarged and shows fewer vesicles.
- 3-No theca lutein cysts.

MICROSCOPY:

- 1-Mild trophoblastic proliferation.
- 2-Hydropsic oedematous cores showing vessels containing fetal erythrocytes.

SERUM CHORIONIC GONADOTROPIN

is lower than in cases of complete mole. +ve

COMPLICATIONS:

- 1-Transformation into invasive mole does not occur and into choriocarcinoma is uncommon.
- 2-Uterine bleeding is less massive.

(X) **INVASIVE MOLE** → form chorio carcinoma + vesicles & abscess formation

Some cases of complete moles (about 15%) show villi that penetrate the myometrium and/or its blood vessels. Penetration may be deep leading to uterine perforation. Deposits "metastatic foci" composed of vesicles may appear in the lung, brain, etc. Invasive mole differs from the usual mole by its invasiveness and from choriocarcinoma by the presence of vesicles and absence of necrosis. The prognosis is much better than choriocarcinoma. Serum chorionic gonadotropin level is high.

Chorio = placenta 2011 (B) **CHORIOCARCINOMA** → من أكثر السرطانات

It arises de novo or on top of invasive mole, complete mole or less commonly partial mole.

GROSS:

- Enlarged uterus. No fetus.
- Large hemorrhagic necrotizing mass, filling the uterine cavity, deeply invading the myometrium.
- Ovaries show theca lutein cysts (see ovarian cysts).

MICROSCOPY:

- Large sheets of malignant cytotrophoblast and syncytiotrophoblast.
- Extensive necrosis and hemorrhage.
- No chorionic villi.

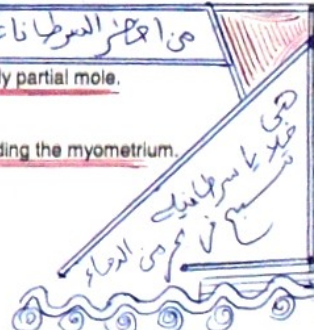
PREGNANCY TEST is positive (high levels of chorionic gonadotropins).

SPREAD:

- Direct spread leading to uterine perforation and massive peritoneal hemorrhage.
- Blood spread is early producing metastases in lungs, bones, liver.
- Lymphatic spread.

What are the hormonal effects of placental tumors

- 1) Positive pregnancy test
- 2) Theca lutein cysts



PLACENTAL SITE TROPHOBLASTIC TUMOR (X)

This is a rare condition that commonly (75%) follow normal pregnancy but it may in some cases be preceded by molar pregnancy. The myometrium shows a mass with little hemorrhage composed of intermediate trophoblastic cells (with features between cytotrophoblast and syncytiotrophoblast). Serum chorionic gonadotropin level is high. The tumor can be distinguished from choriocarcinoma by its monomorphic microscopic pattern (instead of the biphasic cyto- and syncytiotrophoblastic pattern of choriocarcinoma) and also by paucity of hemorrhage (profound in case of choriocarcinoma). The mortality of this tumor is about 10% due to metastases. The prognosis is however better than that of choriocarcinoma.

(B) ECTOPIC PREGNANCY

Definition:

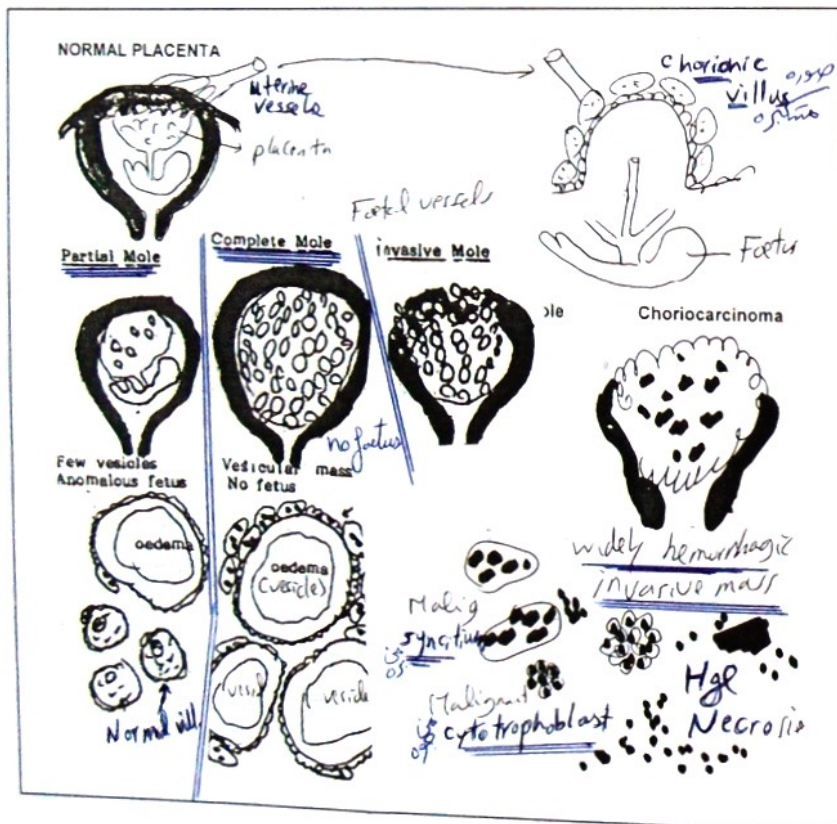
Pregnancy outside the uterine cavity, most commonly in the fallopian tube (tubal pregnancy)

Aetiology:

Mostly due to tubal adhesions (e.g due to chronic salpingitis) which may not prevent fertilization but may interfere with sweeping of the fertilized ovum into the uterine cavity.

Pathology: Chorionic villi and a gestational sac form inside the tube. This leads to tubal rupture and peritoneal hemorrhage & in rare cases this is accompanied by implantation of the fetus in the peritoneum (peritoneal pregnancy). However in the later conditions the fetus dies soon.

Rare sites of ectopic pregnancy: ovary, peritoneum and cervix.



DISEASES OF THE VULVA (B)

VULVAR DYSTROPHIES (X)

These are benign mucosal alterations. The two main varieties are:

1-LICHEN SCLEROSUS: These are whitish lesions of unknown aetiology. They most commonly affect postmenopausal women. Microscopically the lesions show atrophic epidermis with an underlying fibrotic dermis showing chronic inflammation.

2-HYPERPLASTIC DYSTROPHY (Squamous hyperplasia; leukoplakia): These are also whitish lesions. Microscopically the epidermis is hyperplastic. Hyperkeratotic and the dermis shows chronic inflammation. Superimposed dysplasia may occur.

TUMORS OF THE VULVA

BENIGN as papilloma, condyloma acuminatum, sweat gland adenoma, nevus, angioma, lipoma...

Condyloma Acuminatum (anogenital wart):

- Definition:** It is a warty lesion caused by sexually transmitted human papilloma virus.
- Sites:** It affects vulva, vagina, perineum and rarely cervix.
- Gross:** A small or large warty verrucous lesion.
- Microscopy** it consists of papillary proliferation of stratified squamous epithelium with characteristic cytoplasmic vacuolization and nuclear pleomorphism (koilocytosis)

MALIGNANT: Squamous cell carcinoma, melanoma, sarcomas...

Squamous Cell Carcinoma:

- Predisposed** to by vulvar intraepithelial neoplasia.
- Gross:** it forms an ulcerative, polypoid or infiltrative growth.
- Microscopy:** Well to poorly differentiate squamous cell carcinoma.
- Spread** by direct, lymphatic and late blood routes.

VULVAR INTRAEPITHELIAL NEOPLASIA (VIN)

1-VULVAR DYSPLASIA: Also known as vulvar intraepithelial neoplasia (VIN). It is graded as VIN-I, II & III

2-CARCINOMA IN SITU: VIN III or **BOWEN'S DISEASE**

3-PAGET'S DISEASE OF VULVA (Extramammary Paget's disease): It is a special type of carcinoma in situ characterized by vacuolated malignant cells of unsettled origin. It may → aggressive carcinoma

VULVITIS

Vulvitis may be due to sexually transmitted infections (venereal diseases) such as gonorrhea, syphilis, lymphogranuloma venereum, chancroid, herpes virus infection and human papilloma virus infection. Nonsexually transmitted vulvitis includes moniliasis, abscess and others

CYSTS OF THE VULVA

The most common type of vulval cysts are the Bartholin's cysts which often arise due to obstruction of the excretory ducts of these glands.

DISEASES OF THE VAGINA (X)

TUMORS OF THE VAGINA

BENIGN: as Condyloma accuminatum, leiomyoma & hemangioma

MALIGNANT:

1-Squamous cell carcinoma: A rare tumor. Old age. May be related to human papilloma virus infection. Grossly polypoid, ulcerative or infiltrative mass. It spreads by direct routes, lymphatic route (to iliac or inguinal lymph nodes) and rarely by blood.

2-Clear cell adenocarcinoma: A rare tumor that arises in young females (average age 17 years) whose mothers had received treatment with diethylstilbesterol during pregnancy.

3-Embryonal rhabdomyosarcoma (sarcoma botryoides): see before

4-Others as leiomyosarcoma, angiosarcoma, malignant melanoma...etc

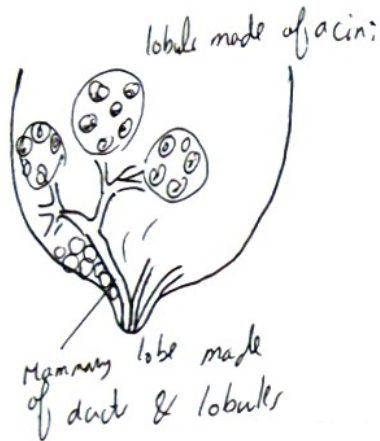
VAGINITIS (x)

Vaginal infections (vaginitis) are uncommon. However **bacterial vaginosis** is not uncommon which is a state of overgrowth of facultative and anaerobic bacterial flora (small coccobacilli)

OTHER VAGINAL DISEASES (x)

- Vaginal intraepithelial neoplasia
- Vaginal cysts as inclusion cysts, Mullerian cysts & mesonephric cysts.
- Vaginal endometriosis

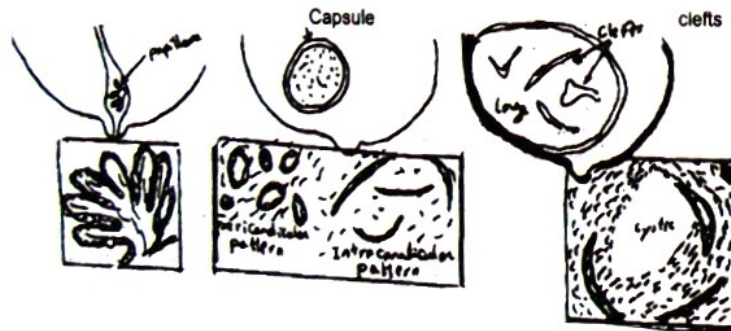
THE NORMAL MAMMARY GLAND



Duct Papilloma

BENIGN MAMMARY TUMORS
Fibroadenoma

Phyllodes tumor



Common in lactation not in pregnancy
① نرم قبل الحمل
② نرم بعد الحمل
③ نرم قبل الحمل و بعد الحمل

CHAPTER XI

DISEASES OF THE MAMMARY GLAND (BREAST)

INFLAMMATORY BREAST LESIONS (MASTITIS) 4

BREAST ABSCESS (Acute suppurative mastitis): Lactational abscess

Aetiology: It usually occurs during lactation. It is due to staphylococcal infection through a fissured nipple, particularly with poor breast hygiene. *Milk retention*

Pathology: Inflammation starts diffuse & the breast appears swollen & painful. Then localization occurs → acute abscess. The abscess is intramammary but may also occur in premammary or retromammary sites. If untreated, it may change into chronic abscess which may be clinically mistaken for a neoplasm.

CHRONIC MASTITIS:

- a) Chronic abscess
- b) Tuberculosis
- c) Actinomycosis
- d) Idiopathic granulomatous mastitis
- e) Syphilis.

DUCT ECTASIA (Periductal mastitis, plasma cell mastitis):

Definition & Aetiology: This is marked dilatation of mammary ducts containing inspissated secretions & surrounded by chronic inflammation rich in plasma cells. It is a relatively common disease mostly occurring above the age of 40 years, but of unknown aetiology.

Gross: A breast mass composed of dilated ducts containing inspissated cheesy secretion

Microscopy: Dilated ducts filled with eosinophilic material, surrounded by lymphocytes, numerous plasma cells, histiocytes and foam histiocytes as well as giant cells and later fibrosis.

FAT NECROSIS: See general pathology.

FIBROCYSTIC DISEASE (FIBROADENOSIS, MAMMARY CYSTIC HYPERPLASIA)

Mammary fibrocystic changes are very common and are thought to represent exaggerated response to hormonal (oestrogen) stimuli. These changes mostly occur at the age of 35-50 years.

GROSS: Site: *upper & middle breast* Aetiology = *repeated anovulatory cycles, oestrogen secreting tumours, oestrogen producing therapy, polycystic ovary + Adrenal hyperfunction*

- May be unilateral or bilateral
- It is characterized by an irregular greyish firm noncapsulated mass or masses with scattered variable-sized cysts ranging between microscopic size and few centimeters. The cysts contain clear or hemorrhagic fluid & may appear yellowish, brownish or blue.

MICROSCOPY: There is a variable mixture of the following changes:

1-Epithelial Hyperplasia:

- **Adenosis:** This is increased number of acini/ductules → increased size of the lobules.
- **Lobular hyperplasia:** The cells lining the acini are hyperplastic forming many layers that may occlude the acinar lumens. This may be associated with cellular atypia (atypical lobular hyperplasia).
- **Ductal hyperplasia (epitheliosis):** The ducts are lined by many layers of cells (epitheliosis), sometimes with papillary formation (papillomatosis). Epithelial hyperplasia may be associated with atypia (atypical ductal hyperplasia).

2-Cysts: These are dilated ducts containing secretions.

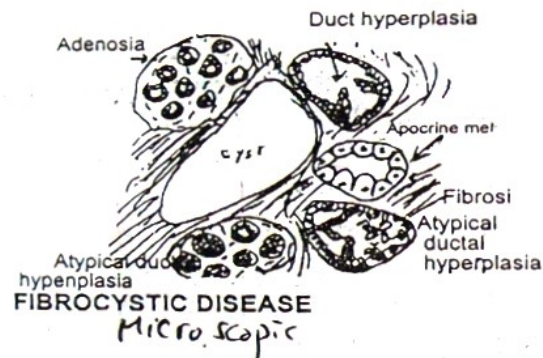
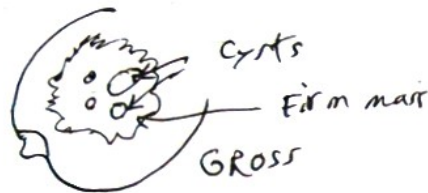
3-Apocrine metaplasia: The lining of cysts frequently undergo apocrine metaplasia, (large with abundant eosinophilic cytoplasm resembling cells of the apocrine sweat glands).

3-Fibrosis.

4-Sclerosing adenosis: It characterized by adenosis & extensive fibrosis that distorts and compresses the hyperplastic ductules giving a false impression of invasive cancer. Identification of myoepithelial cells within the compressed ductules differentiates this benign condition from breast carcinoma.

RELATION TO CARCINOMA:

The risk of carcinoma is increased in cases of fibrocystic disease; particularly in the presence of atypical lobular & ductal hyperplasia (5 times risk of cancer development more than in normal breasts)

FIBROCYSTIC DISEASE**BENIGN TUMORS OF THE BREAST****1-DUCT PAPILLOMA**

Usually in middle aged females.

Gross: A small pedunculated branching mass.

Microscopy: Vascular cores covered by columnar cells.

Effects: 1) Bleeding per nipple. 2) Malignant change.

2-FIBROADENOMA

It is the most common benign tumor of the breast. It occurs in young age groups; 15-25 years. Malignant change is extremely uncommon and exceptional.

Gross:

A capsulated, rounded or oval mass, ranging in diameter from less than 1 cm to more than 10 cm (the later is called giant fibroadenoma). It is usually single, but more than one tumor may occur. Cut section is uniform grayish white and may show slits. The commonest site is the upper outer quadrant of the breast.

Microscopy:

The tumor consists of proliferated ductules lined by regular epithelium and myoepithelium and surrounded by abundant fibroblastic stroma. The ductules may be patent with recognizable lumens, in such conditions the tumor is termed pericanalicular fibroadenoma. The stroma may be so abundant that the ductules become compressed and appear slit-like, in such conditions the tumor is termed intracanalicular fibroadenoma. A mixture of peri and intracanalicular patterns is not uncommon. There is no difference in clinical behavior between pericanalicular and intracanalicular types.

Relation to carcinoma: Malignant change in fibroadenoma is extremely rare, & when present it is usually an in situ carcinoma.

3-PHYLLODES TUMOR

This uncommon tumor usually occurs in middle-aged females. It was formerly called cystosarcoma phyllodes, but this term is disliked since most tumors are benign.

Gross: A capsulated large mass; 10-15 cm in diameter. Cut section shows myxomatous and cystic areas as well as leaf-like clefts and slits (phyllodes).

Microscopy: It resembles intracanalicular fibroadenoma, but the stroma is very cellular.

Effects:

- 1-Breast enlargement.
- 2-Malignant phyllodes (uncommon) may occur on top of benign phyllodes tumor (as evidenced by increased mitotic activity of the stromal cells & infiltrative margins), or de novo. The malignant elements are the stromal cells (sarcomatous) which metastasize mainly by blood spread.

4-OTHER BENIGN TUMORS

Lipoma, hemangioma, neurofibroma.... Etc.

CARCINOMA OF THE BREAST

Mammary carcinoma is the commonest form of malignancy in females. On the other hand the other forms of malignancy (malignant phyllodes tumor, sarcoma and secondaries) are rare.

RISK FACTORS & PRECANCEROUS LESIONS:

- 1-Heridity (the responsible genes are called BR CA genes).
- 2-Early menarche and/or late menopause.
- 3-Nulliparity.
- 4-Endogenous hyperoestrogenism (50% of mammary carcinomas are oestrogen dependent).
- 5-Obesity: Higher risk due to local synthesis of oestrogen within the fat depot (including mammary fat).
- 6-Carcinoma of one breast increases the risk of cancer development in the contralateral breast.
- 7-Fibrocystic disease with atypical hyperplasia.
- 8-Duct papilloma.
- 9-Milk factor (virus): Only in experimental animals.

AGE: Most carcinomas occur above the age of 40 years. However, younger ages can be affected. In rare cases children are affected (juvenile carcinoma).

SITES:

- 1-Upper outer quadrant: 50%
- 2-Central compartment: 20%
- 3-Rest of breast: 30%

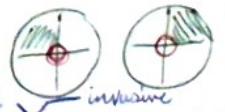
CLASSIFICATION:

A-CARCINOMAS OF LOBULAR ORIGIN: Less than 10% of cases.

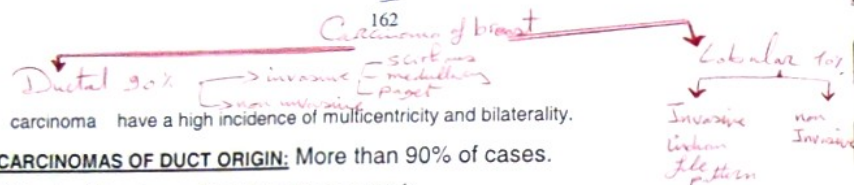
- 1) **Lobular Carcinoma In Situ:** The acini are distended with small malignant cells with no invasion of their basement membrane. May ultimately change into invasive lobular carcinoma.
- 2) **Infiltrating (Invasive) Lobular Carcinoma:** There are small malignant cells typically invading the stroma in the form of linear cords (Indian File Pattern). Both insitu and infiltrating lobular

VSP+A+ Jax+Case + Pathology
2011

50% upper outer
20% central
30% rest



Lobular 10%
duct 90%
invasive
non invasive (insitu)



B-CARCINOMAS OF DUCT ORIGIN: More than 90% of cases.

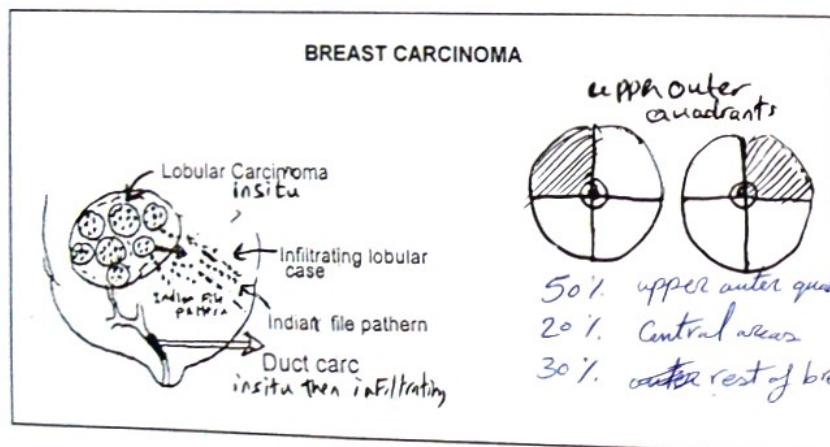
1) Intraduct Carcinoma (Duct Carcinoma Insitu):

Gross: The tumor appears grossly as a noncapsulated mass composed of enlarged ducts, many of which contains yellowish necrotic material. When the mass is squeezed, this necrotic material comes out of the cut surface of the mass like a tooth paste.

Microscopy: The ducts are enlarged and lined by several layers of malignant cells without invasion of the basement membrane. The intraductal cell proliferation may assume several patterns including a cribriform pattern, a papillary pattern and a comedo pattern. The later pattern appears as central eosinophilic necrosis filling the lumen of the ducts and surrounded peripherally by few layers of malignant cells. This comedo pattern (intraduct comedo carcinoma) is more rapidly followed by infiltration (infiltrating comedo carcinoma).

Prognosis:

- 1-The tumor is noninvasive & is cured by surgery.
- 2-Incidence of multicentricity and bilaterality is high.
- 3-If not treated, it may be followed by invasion (infiltrating duct carcinoma).



2) Infiltrating Duct Carcinoma: Several patterns:

a) Infiltrating Duct Carcinoma Not Otherwise Specified (NOS): It was formerly known as Scirrhous Carcinoma. It is the most common type; more than 2/3 of breast cancer.

Gross: the tumor appears as an ill-defined hard grayish mass that gives a gritty sensation on cutting. The cut surface retracts. The following features are commonly encountered (but may also occur with other types of breast carcinoma):

- 1-Retracted of the nipple or skin dimpling due to adherence of the tumor to the overlying skin and retraction of the fibrotic stroma of the tumor.
- 2-Peau d'orange: Mammary skin appears mamillated (like the peel of an orange) due to lymphoedema (caused by lymphatic obstruction) which leads to forward pushing of the skin except at points of skin anchorage (points of attachment of adenexa) which appear depressed giving the skin a "peau d'orange" appearance.
- 3-Cancer en cuirasse: This is hardening and fixation of the breast due to lymphoedema and invasion of pectoral muscles.
- 4-Inflammatory Carcinoma: Sometimes (particularly during pregnancy) extensive lymphatic invasion occurs associated with an acute inflammatory reaction leading to swelling, redness and tenderness of the breast; which may be mistaken for acute mastitis.
- 5-Microcalcifications (detected by mammography) in about 60-70 % of breast carcinoma

Microscopy: The tumor consists of small groups of medium sized malignant cells, associated with (dense stromal sclerosis.) desmoplasia.

b) Medullary Carcinoma: ~ Better prognosis because infiltrated by lymphocytes

Grossly, the tumor appears as a fairly defined (expansile) soft mass with areas of necrosis and hemorrhage. The cut surface bulges.

Microscopically, the tumor consists of large sheets of large-sized malignant cells showing high grade of anaplasia and frequent mitoses. The stroma is scanty & intensely infiltrated by lymphocytes.

Prognosis: Medullary carcinoma with lymphocytic infiltrates has a much better prognosis than scirrhous carcinoma.

c) Paget's Disease of Breast:

The disease is characterized by 2 features:

- Mammary carcinoma: Intraduct or invasive (of any pattern).
- Eczema of the nipple due to transductal intraepidermal spread.

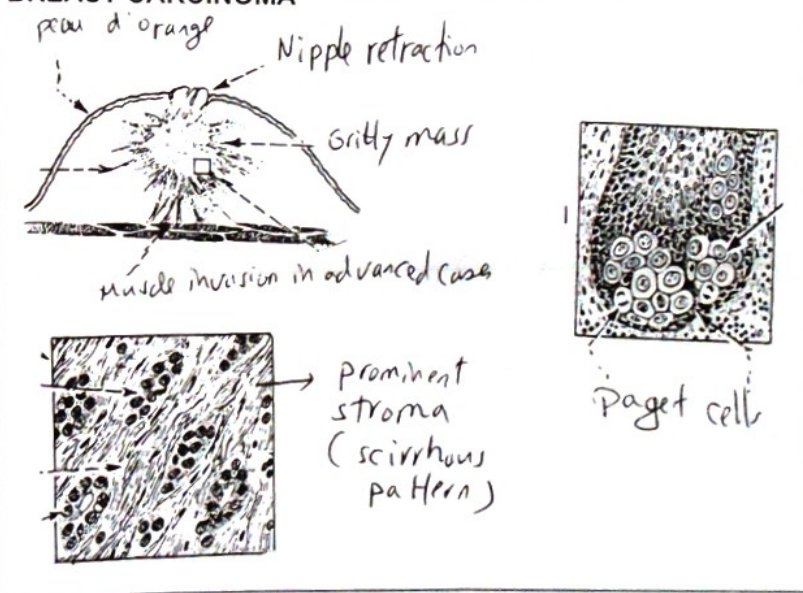
Grossly: The nipple is red, ulcerated and scaly.

Microscopically: The epidermis is infiltrated by large-sized neoplastic cells with clear cytoplasm and large hyperchromatic nuclei. These cells are called Paget's cells.

d) Other Types:

- 1-Tubular and adenocystic carcinomas: The prognosis of these tumors is relatively favorable.
- 2-Mucoid carcinoma: Grossly a gelatinous mass. Microscopically consists of malignant cells with large pools of mucin. The prognosis of mucoid carcinoma of the breast is relatively favorable (in contrast to the poor prognosis of mucoid carcinoma in other sites of the body).
- 3-Juvenile (secretory) carcinoma: This rare tumor of children has an excellent prognosis.
- 4-Apocrine carcinoma.
- 5-Carcinoma with neuroendocrine differentiation.

BREAST CARCINOMA



SPREAD:

A) **Local Spread** to skin and chest wall.

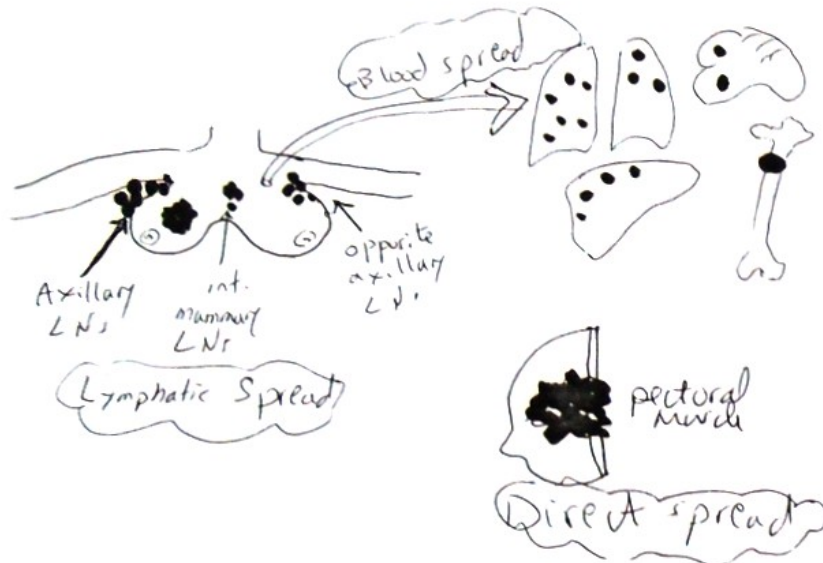
B) **Lymphatic Spread:**

1- **Lymphatic Emboli** lead to metastases in axillary lymph nodes. Further spread leads to metastases in intraclavicular and sometimes supraclavicular nodes. Internal mammary nodes may be also involved.

2- **Lymphatic Permeation:** It leads to lymphoedema causing:

- Peau d'orange: describe
- Cancer-en-cuirasse: describe

C) **Blood Spread:** This leads to distant metastases in lungs, liver, bone...etc.

SPREAD OF BREAST CARCINOMA**TNM STAGING OF BREAST CANCER:**

- Tis: In situ lobular or duct carcinoma.
- T1: Tumor 2 cm or less in longest dimension.
- T2: Tumor 2-5 cm in longest dimension.
- T3: Tumor more than 5 cm in longest dimension.
- T4: Tumor of any size with invasion of skin or chest wall.
- N0: No lymph node metastases.
- N1: Metastases to ipsilateral axillary lymph nodes without fixation.
- N2: Metastases to ipsilateral lymph nodes, with fixation.
- N3: Metastases in ipsilateral infraclavicular or supraclavicular nodes.
- M0: No evidence of distant metastases.
- M1: Distant metastases.

(X) **ESTROGEN RECEPTORS (ER), PROGESTERONE RECEPTORS (PR) and HER2:**

- Tumor cells may be positive for ER & PR (& negative for Her2) → this allows treatment with anti hormones (tamoxifen) → better control of tumor growth & better prognosis
- Tumor cells may be negative for hormone receptors & often positive for Her2 which denotes higher capability of tumor cells to spread. Such tumors need aggressive chemotherapy

SARCOMAS OF THE BREAST

These are rare tumors. Rare. Examples: Malignant phyllodes tumor, fibrosarcoma, angiosarcoma, malignant fibrous histiocytoma, liposarcoma.

DISEASES OF THE MALE BREAST**CARCINOMA OF MALE BREAST**

Rare. Same types as female breast cancer. Infiltrating carcinoma has a poor prognosis because the small size of the male breast allows early invasion of chest wall and hence early invasion of lymphatics and blood.

GYNAECOMASTIA

This is unilateral or bilateral breast enlargement in males.

Aetiology:

- Excess oestrogen due to:
 - * *digitalis* (tumor e.g. Sertoli cell tumor)
 - * *idiopathic* (oestrogen therapy e.g. cancer prostate)
- Excess oestrogen due to:
 - a) Liver failure.
 - b) Oestrogen therapy for cancer prostate.
 - c) Sertoli cell tumor of testis.

2- Prolonged treatment with some drugs as digitalis.

3- Idiopathic (unknown cause).

Pathology:

Gross: Firm rubbery breast mass.

Microscopy: Duct hyperplasia and fibrosis.

BLEEDING PER NIPPLE

- Duct papilloma.
- Duct carcinoma.
- Mammary hyperplasia.
- General causes of bleeding.

TYPES OF BREAST MASSES**Neoplastic Disease:**

- Benign tumors
- Malignant tumors.

Hyperplastic Disease: Fibrocystic disease (mammary hyperplasia)

Inflammatory Disease as

- Chronic abscess,
- Mammary duct ectasia,
- Tuberculous mastitis...etc.

Traumatic Lesions:

- Fat necrosis
- Hematoma

Male	vs	Female
♂ duct only		♀ duct + Lobules
rarely cancer breast but fatal		Common cancer breast can be treated

DISEASES OF BONES AND JOINTS

OSTEOMYELITIS

Bone inflammation
= Bone + Bone marrow

Definition: This is inflammation of bone and bone marrow

Classification:

A) **Bacterial:**

1) **Acute osteomyelitis** (acute suppurative osteomyelitis):

- a) Acute hematogenous osteomyelitis
- b) Acute non-hematogenous osteomyelitis

2) **Chronic osteomyelitis:**

- a) Chronic nonspecific (suppurative) osteomyelitis
- b) Chronic specific osteomyelitis (tuberculous, syphilitic)

B) **Non-bacterial** e.g

- 1) Viral osteomyelitis
- 2) Sarcoidosis
- 3) Radiation osteomyelitis

ACUTE HEMATOGENOUS OSTEOOMYELITIS

A+V IP+SP
+ Jacc
+ Case

Aetiology & Pathogenesis: Most common in children:

- The organisms: Staph. aureus in 80-90% of cases, less commonly others as E.coli, Salmonella, Staph. albus, Pneumococci or Streptococci.

- **Source of infection:** The organisms are derived from remote infections (respiratory, intestinal, urinary, oral, skin, etc). They reach the blood (bacteraemia) following trivial injuries such as intestinal mucosal abrasions during defecation or slight oral mucosal injuries due to vigorous chewing of hard foods.

The bones most commonly affected by blood spread are the long bones followed by the vertebrae. The location of the lesions within the affected long bone is influenced by the vascular circulation, which changes with age. In children, bone infection is typically metaphyseal, because this is the most vascular part of bone and because the blood flow within the metaphysis is normally slow, moreover, metaphysis is the most common part of bone subjected to trauma (trauma is known to be a predisposing factor). In infants and adults, the epiphysis may be also affected.

Pathological Features:

- 1- The initial lesion is a **suppurative focus in the metaphysis**.
- 2- Spread of infection occurs by penetrating the **endosteum** reaching the **Haversian system** through which the organisms reach the **periosteum** → **subperiosteal abscess**. Rupture of the subperiosteal abscess → **sinuses**.
- 3- **Bone necrosis** due to:
 - a) Bacterial toxins.
 - b) Ischemia due to stretching, compression or thrombosis of periosteal vessels.
- 4- Separation of the necrotic bone by action of **osteoclasts**. This separated part is called **sequestrum**. The margins of this sequestrum are serrated.
- 5- Gradual thickening of the periosteum due to new bone formation (**involucrum**). The sinuses now appear as thick-walled holes called **cloacae**. This occurs in the chronic phase.

Complications:

- 1- Pathological fracture.
- 2- Direct spread of infection → a) arthritis b) myositis c) neuritis...
- 3- Blood spread of infection → toxemia, septicaemia and pyaemia.
- 4- Chronic suppurative osteomyelitis. This may be further complicated by:
 - a- Secondary amyloidosis
 - b- Epithelialization of the sinuses which may later give rise to squamous cell carcinoma.

Antibiotic → علاج

ACUTE NON-HEMATOGENOUS OSTEOOMYELITIS

Aetiology:

- 1- Infection of a fractured bone.
- 2- Infection of skull bones due to direct spread e.g mastoiditis in case of otitis media.

Pathology: It resembles the pathology of the hematogenous type except for different location (sites of fracture and skull bones) and usually absent subperiosteal abscess.

no subperiosteal abscess
→ through fracture bone
→ skull bone direct spread
oral + MCQ

CHRONIC NONSPECIFIC OSTEOOMYELITIS

oral + MCQ

1- Chronic osteomyelitis following acute osteomyelitis.

2- **Brodie's Abscess:**

- It is a localized form of osteomyelitis caused by Staphylococcus aureus.
- It starts chronic with no preceding acute phase.
- It appears as a small intra-osseous, frequently cortical abscess surrounded by reactive sclerotic bone.
- It is more common in young age.
- It may be complicated by pathological fracture, nearby joint effusion and amyloidosis.

2- **Sclerosing osteomyelitis of Garre:** It typically develops in the jaw and is characterized by extensive new bone formation.

TUMORS OF BONES

ORIGIN	BENIGN	LOCALLY MALIG	MALIGNANT
Osteogenic Tumors (from osteoblasts)	Osteoma. Osteoblastoma.		Osteosarcoma.
Chondrogenic Tumors (from chondroblasts)	Chondroma. Chondroblastoma Chondromyxoid fibroma		Chondrosarcoma.
Developmental	Osteochondroma		
Fibroblastic Tumors	Fibroma.		Fibrosarcoma.
Notochordal remnants		Chordoma.	Chordoma.
Epithelial		Adamantinoma.	Adamantinoma
Vascular	Hemangioma.		Angiosarcoma.
Neurogenic	Schwannoma.		Malig. schwannoma
Adipose Tissue	Lipoma.		Liposarcoma.
Bone Marrow			Myeloma Lymphoma leukemia
Unsettled Origin		Giant cell tumor	Giant cell tumor. Ewing's sarcoma
Fibrohistiocytic	Benign fibrous histiocytoma		Malignant fibrous histiocytoma.
Secondary Tumors			Metastases

BENIGN TUMORS OF BONE

- 1) **Osteoma & osteoblastoma:** See general pathology.
- 2) **Osteochondroma (exostosis):** See general pathology.
- 3) **Chondroma:** See general pathology
- 4) **Chondroblastoma**
 - It is an uncommon benign epiphyseal tumor of long bones of young adults.
 - Grossly: It appears as a grayish pink growth expanding the affected end of long bone.
 - Microscopically: Immature looking cartilage with characteristic "chicken wire" calcifications.

Chondroblastic
MCQ
paper 2

5) Chondromyxoid fibroma:

- An uncommon benign tumor of young adults, commonest in metaphysis of long bones.
- It consists of a mixture of cartilage, myxoid and fibrous tissue arranged in lobules

6) Fibroma: This lesion may be:

- Non-ossifying fibroma** (also called metaphyseal fibrous cortical defect and benign fibrous histiocytoma). This tumor affects the metaphysis of long bones and consists of proliferated benign spindle cells as well as multinucleated giant cells and histiocytes.
- Ossifying fibroma** (also called osteofibrous dysplasia): It predominantly affects the tibia of young children and is characterized by a mixture of proliferating spindle cells and active bone formation
- Cemento-ossifying fibroma** (cementoma): It affects craniofacial bones and consists of a mixture of proliferating spindle cells and globules of osteoid tissue that resemble cementum

Remark: Both of ossifying fibroma and cemento-ossifying fibroma are nowadays considered as variants of fibrous dysplasia (see later).

7) Other benign tumors as hemangioma & intra-osseous lipoma.

LOCALLY MALIGNANT TUMORS OF BONE

1-GIANT CELL TUMOR (OSTEOCLASTOMA)

Locally malignant neoplasm of unsettled origin
Age: Usually after the age of 20 years but may occur in younger ages.

Origin and Sites:

Most giant cell tumors are locally malignant. Few cases (10-20%) are malignant and metastasize. The tumor consists of a mixture of giant cells (which proved to be non neoplastic) and neoplastic mononuclear stromal cells of unsettled origin (believed to be osteoblastic or fibroblastic). The most common sites are around the knee joint (distal femur and proximal tibia).

Gross Features:

The tumor involves both epiphysis and metaphysis. It usually forms an eccentric mass that erodes the subchondral bone. The covering cortical bone becomes markedly thinned (egg shell-like). The tumor tissue is grayish brown and frequently shows cystic degeneration. Areas of hemorrhage are common.

Microscopic Features:

- Mononuclear tumor cells: These are oval mononuclear stromal cells showing dark nuclei with grades of atypia ranging between mild & marked.
- Multinucleated giant cells (up to 100 nuclei); osteoclastic type. All evidences suggest that these cells are non-neoplastic and develop by fusion of monocytes-macrophages.
- Collagenous stroma, vessels and areas of hemorrhage.

Radiological Features: Classically giant cell tumor appears as an eccentric lytic lesion with an adjacent thinned cortex and with minimal or no periosteal reaction.
Spread: 80-90% of cases spread locally. The remaining cases may have a malignant behaviour and metastasize by blood.

2-ADAMANTINOMA

1-ADAMANTINOMA OF MANDIBLE OR MAXILLA (Ameloblastoma):

- A locally malignant tumor arising from ameloblasts (tooth epithelium).
- Pathology: Grossly: An intra-osseous or peripheral, solid or multilocular cystic mass, resembling giant cell tumor. Microscopically it consists of islands of odontogenic epithelium in a fibrous stroma.
- Distant metastases are rare.

2-ADAMANTINOMA OF LONG BONES:

This tumor is locally malignant (80%) or malignant metastasizing (20%). Tibia is the most common site. The tumor consists of nests of epithelium in a fibrous stroma. The origin of the tumor is unsettled.

3-CHORDOMA

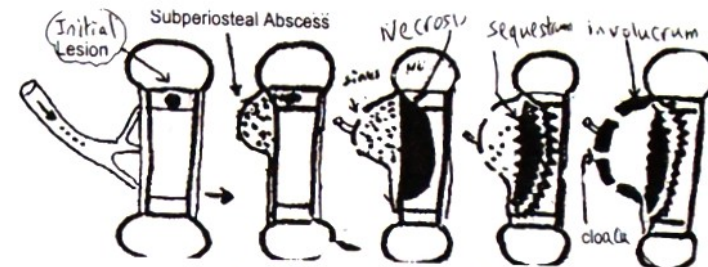
It is a locally malignant (or malignant) tumor, mostly occurs above the age of 40 years. It arises from notochordal remnants.

The most common site (50%) is the sacrococcygeal region.

Grossly the tumor appears as an infiltrative gelatinous mass.

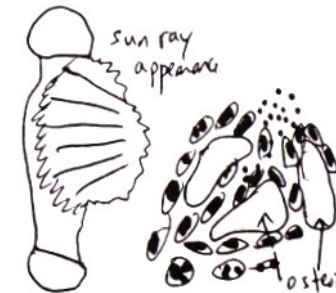
Microscopically it consists of cells with vacuolated cytoplasm and vesicular nuclei (physaliferous cells).
Prognosis: Local recurrences after treatment are common. Finally the tumor sends distant metastases

OSTEOMYELITIS



Acute Hematogenous Osteomyelitis

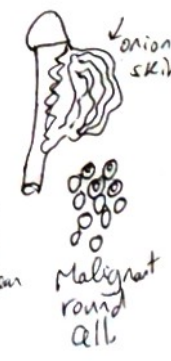
OSTEOSARCOMA



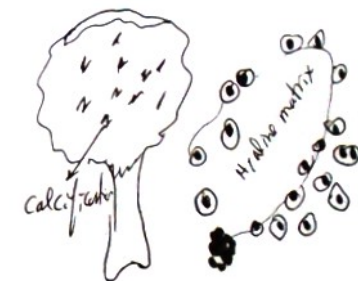
GIANT CELL TUMOR



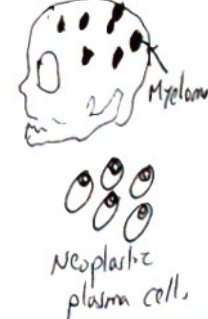
EWING SARCOMA



CHONDROSARCOMA



MULTIPLE MYELOMA



MALIGNANT TUMORS OF BONE

1-OSTEOSARCOMA (Osteogenic sarcoma)

Origin and Sites: This is the most common primary malignant tumor of bone. The neoplastic cells are osteogenic i.e. secrete bone matrix (osteoid and/or osseous tissue). Any bone may be affected, but the most common sites include distal femur and proximal tibia (ends of bone around knee joint; 60%), proximal femur (15%) and proximal humerus (10%). The tumor starts within the metaphysis.

Age:

- Children and young adults, usually below 20 years.
- Osteosarcoma may also occur in the elderly on top of Paget's disease.

Predisposing Factors:

- 1-Trauma.
- 2-Irradiation.
- 3-Paget's disease of bone.
- 4-Fibrous dysplasia.
- 5-Osteochondroma.

Gross Features:

- The tumor forms a large mass that extends within the medullary canal and destroys the bone cortex.
- The periosteum is elevated then becomes penetrated and extension within the adjacent soft tissue occurs. Hemorrhage and necrosis are usually extensive.
- Well differentiated tumors are usually hard (osteosclerotic), while undifferentiated tumors are usually soft (osteolytic).

Microscopic Features:

- Tumor cells** are pleomorphic and include spindle and giant cell forms with large dark nuclei showing abnormal mitotic activity.
- Matrix** consists of osteoid tissue; which is prominent in better differentiated tumors, but minimal in poorly differentiated tumors. There may be also collagenous and cartilaginous matrices.
- Thin-walled vessels** are present and may be very numerous (telangiectatic osteosarcoma). Areas of necrosis and hemorrhage are frequent.

Radiological Features:

- 1-Tumors rich in bone matrix may exhibit sun ray appearance in X ray films.
- 2-Periosteal elevation may be associated with reactive periosteal bone formation in the triangle between the cortex and elevated periosteum. This can be detected in X ray films and is called Codman's triangle.

Spread & prognosis: A highly malignant tumor → rapid spread & poor prognosis:

- 1-Direct spread to the surrounding soft tissues
- 2-Blood → metastases in lung & other distant sites.

(X) UNCOMMON TYPES OF OSTEOSARCOMA:

1-Juxtacortical (parosteal) osteosarcoma: The tumor arises in the juxtacortical areas of long bones and forms a grayish mass encircling the bone. Microscopically there are spindle cells with little anaplasia accompanied by well formed osseous and osteoid bone and sometimes cartilage. The prognosis of this tumor is very good.

2-Periosteal osteosarcoma: The tumor arises from the periosteum. It is an osteosarcoma with cell anaplasia intermediate between the classical ad juxtacortical types. The tumor is also characterized by a prominent cartilaginous component.

2-CHONDROSARCOMA

Chondrosarcoma is less common than osteosarcoma

primary malignant neoplasm arising from chondrogenic cells

Origin and Sites:

- It is a malignant neoplasm characterized by chondrogenic cells i.e. secreting cartilaginous matrix.
- Arise in any bone, but most commonly in the central portions of the skeleton (pelvis, shoulder & ribs).

Age: The 4th decade is the most common, but younger and older ages may be affected.

Predisposing Factors:

- 1)Paget's disease of bone.
- 2)Fibrous dysplasia.
- 3)Chondroma and osteochondroma.

Gross Features: The tumor grows within the medullary canal. Low grade tumors cause reactive thickening of the cortex, but high grade tumors penetrate the cortex and periosteum and extends into the adjacent soft tissues forming a large mass with areas of necrosis and hemorrhage. Myxomatous and calcific changes are common.

Microscopic Features:

- Tumor cells:** In low grade tumors; the chondrocytes show mild atypia and minimal mitoses; but in high grade tumors there is marked pleomorphism, large dark nuclei and frequent mitoses.
- Hyaline matrix** is more abundant in low grade tumors. Myxoid change and spotty calcifications are common.
- Vascularity**, hemorrhage and necrosis are more obvious in high grade tumors.

Radiological Features: Mottled densities (due to spotty calcifications) are commonly detected.

Spread:

- 1-Low grade chondrosarcoma spreads locally with no distant spread.
- 2-High grade chondrosarcoma spreads locally and by blood (similar to osteosarcoma).

Prognosis: Generally better than osteosarcoma

3-FIBROSARCOMA

Origin & Sites: Fibrosarcoma is an uncommon bone tumor that arises from the periosteum (and rarely medullary canal). The femur and tibia are the most common sites.

Age:

Adults

Gross:

- Periosteal fibrosarcoma surrounds the bone and may infiltrate the bone cortex.
- Medullary osteosarcoma expands the medullary canal and erodes the cortex and periosteum

Microscopy: Pleomorphic spindle cells with low grade or high grade nuclear atypia, collagenous matrix & thin walled blood vessels. Hemorrhage and necrosis are more common in high grade tumors.

Radiology:

Spread & prognosis: Slower in low grade (well differentiated) tumors which have better prognosis. High grade tumors spread by direct and blood routes.

4-PLASMA CELL NEOPLASMS

A) MULTIPLE MYELOMA:

Age: Commonly above the age of 40 years.

Origin: A malignant plasma cell tumor occurring in bone marrow.

Sites: Skull, vertebrae, sternum, pelvis and ribs.

Gross features: Often arise as multiple tumors (myelomatosis). May rarely start as a solitary myeloma, but sooner or later become multiple. The tumors appear as soft red nodules.

Microscopy: Atypical (malignant) plasma cells; at different stages of maturation.

Radiology: Multiple osteolytic defects.

Effects:

1-Bone and bone marrow destruction leading to:

- a)Pathological fractures.
- b)Pancytopenia.
- c)Hypercalcaemia and metastatic calcifications.

Chondroma	vs	Chondrosarcoma
no blood vessel		blood vessels
no permeating not necrosis		permeating + necrosis

perosteal osteosarcoma
medullary osteosarcoma

Site Multiple at axial skeleton

Renal failure

renal failure without hypotension due to amyloidosis
 Multiple Myeloma 172
 Congulate then dissolve if continue heating

2-Production of abnormal immunoglobulins (Bence-Jones proteins) leading to:
 a) Bence-Jones proteinuria. These proteins form casts that block the tubules. They can be detected in urine by heating since these abnormal proteins coagulate at 55°C & are dissolved on continuing heating at 85°C.
 b) Low immunity leading to intercurrent infections.

c) Amyloidosis (25% of cases).

3-Blood spread (plasma cell leukemia)

4-Renal changes (myeloma nephrosis) are common leading to renal failure. They include block of renal tubules by casts. Nephrocalcinosis and pyelonephritis are common.

B) SOLITARY PLASMOCYTOMA: A solitary plasma cell tumor composed of sheets of plasma cells in a well vascularized stroma. Can affect any bone or soft tissue. One third of treated cases progress to multiple myeloma.

C) PLASMACYTOID LYMPHOMA (WALDENSTROM'S MACROGLOBULINEMIA): This is a syndrome of plasmacytoid B cell lymphoma, associated with hyperglobulinemia (macroglobulinemia) leading to increased blood viscosity. Hepatosplenomegaly and lymphadenopathy, anemia and neurologic abnormalities are frequent findings. The disease mainly affects elderly persons.

5- EWING'S SARCOMA

Origin and Sites:

The origin is unsettled; recently believed to be of neural origin.

It usually arises in the medullary canal of the diaphysis of long bones especially the femur or in the flat bones of the pelvis. It may also arise in soft tissues (& is called primitive neuroectodermal tumor; PNET).

Age: 5-20 years, but may occur in older age groups (mainly PNET).

Gross Features: A soft mass with extensive necrosis and hemorrhage that destroys the bone cortex.

Microscopic Features: Round cells with dark nuclei that may be confused with other malignant round cell tumors such as lymphoma or neuroblastoma, but their cytoplasm characteristically contains glycogen.

Radiological Features: A lytic destructive bone lesion with a characteristic periosteal reaction in the forms of layers of reactive bone deposited in an onionskin-like fashion.

Spread: Direct and by blood.

Remark: Ewing's sarcoma usually present as a painful tender swelling that may be clinically confused with osteomyelitis. Biopsy & microscopic examination easily recognize the lesion.

OSTEODYSTROPHIES

Abnormalities of bone growth and structure

1-FIBROUS DYSPLASIA

This disorder can affect any bone at any age.

Pathology: The disease has three patterns:

1-Monostotic: single bone involvement.

2-Polyostotic: Multiple but never all bones.

3-Albright syndrome: polyostotic with café au lait skin pigmentations and precocious puberty.

In any of these patterns, the affected bone grossly shows medullary fibrous proliferation which appears grayish and gritty associated with cortical thinning. Microscopically there is fibrous tissue proliferation trapping thin irregular bone trabeculae.

Complications: 1) Pathological fracture 2) Sarcomatous transformation.

Osteitis deformans

2-PAGET'S DISEASE

Aetiology: A disease of unknown aetiology, affecting old males. Very rare in Egypt.

Pathogenesis: Bone decalcification followed by excess deposition of weak bone → bone thickening

Pathology: It is characterized by a "collage of matrix madness" where the affected bone or bones show:

- 1-Areas of furious osteoclastic bone resorption (osteolytic phase) followed by
- 2-A period of hectic bone formation (osteoblastic phase).
- 3-The net result is increased bone density (osteosclerotic stage) → bone deformities as
 - a) Skull enlargement with narrowing of its foramina
 - b) Bending of long bones.

Complications:

- 1) Pathological fracture
- 2) Sarcomatous transformation (osteosarcoma, chondrosarcoma or fibrosarcoma)
- 3) High output heart failure may also complicate the disease.

3-OSTEOPOROSIS

Definition: Decreased mass of normally mineralized bones, usually due to increased bone absorption

Causes: 1) Senility 2) Post menopausal women 3) Decreased mobility (e.g due to paralysis) 4) Cushing syndrome 5) Prolonged corticosteroid therapy.

Pathology: Bones are thinned.

Complications: 1) Pathological fractures are common. 2) Vertebral deformities may occur.

4-OTHERS

Hyperparathyroidism, rickets, osteomalacia, osteogenesis imperfecta, achondroplasia.

CAUSES OF PATHOLOGICAL FRACTURE

- 1) Inflammatory disease (acute osteomyelitis, chronic osteomyelitis... enumerate types).
- 2) Osteodystrophies: Osteoporosis, hyperparathyroidism, rickets, osteomalacia, fibrous dysplasia, Paget's disease.
- 3) Primary malignant tumors
- 4) Metastases
- 5) Bone cysts (as aneurysmal cyst & hydatid cyst)

BONE CYSTS (x)

1-Unicameral bone cyst: May result from a local developmental defect, commonly metaphyseal affecting long bone in children and young adults. The cyst is lined by connective tissue with histiocytes and haemosiderin deposition.

2-Aneurysmal bone cyst: Thought to result from altered hemodynamic of bone or as a result of arteriovenous fistula. It appears as a large destructive lesion causing expansion of bone, usually affects vertebrae and flat bones. It is multilocular and hemorrhagic with a thin rim of bone at outer surface. Microscopically, shows large endothelial lined hemorrhagic spaces surrounded by proliferating spindle cells and numerous osteoclast-like giant cells.

3-Epidermoid cyst

4-Ganglion cyst of bone

5-Hydatid cyst

6-Osteitis fibrosa cystica

ARTHRITIS

Acute
chronic
= inflammation of joints

Inflammation of joints (arthritis) is classified into the following types: ^{P.4}

- 1) **Acute arthritis**: a) suppurative b) traumatic c) rheumatic d) viral & e) acute gouty arthritis
- 2) **Chronic arthritis**: a) osteoarthritis (osteoarthrosis), b) rheumatoid arthritis c) chronic gouty arthritis, d) pseudogout (acute self-limiting arthritis due to deposition of calcium pyrophosphate of unknown cause) e) tuberculous arthritis (see general pathology) f) syphilitic arthritis g) Neuropathic arthritis (Charcot's arthritis) h) Hemophilic arthritis

SUPPURATIVE (SEPTIC) ARTHRITIS

(X)

Aetiology: It is an acute inflammation that commonly involves a single large joint such as the knee or hip

Organisms: Staphylococcus aureus, less frequently Streptococci and Haemophilus-influenza

Route of infection: 1) By direct spread from adjacent osteomyelitis, 2) following penetrating injury 3) Blood borne infection may also occur

Pathology:

- Suppurative inflammation of synovial membrane, capsule, ligaments & surrounding soft tissue.
- Joint is swollen with purulent exudate (pus) associated with severe pain, tenderness, redness, swelling, local warmth & marked restriction of movement
- Destruction of articular cartilage may occur → healing → fibrous ankylosis or rarely bony ankylosis

RHEUMATOID ARTHRITIS

DEFINITION:

It is an autoimmune collagen disease, more common in females between 30-50 years.

PATHOGENESIS:

An autoimmune mechanism of unknown stimulus (? post-viral or bacterial). Autoantibodies are liberated and excite an inflammatory reaction. The inflammatory cells release cytokines as TNF & interleukins as well as enzymes as proteases → destruction of joint structures.

PATHOLOGY: Articular (joint) & extra-articular lesions:

- 1) **Joint (Articular) Lesions**: It is a polyarthritis, mainly involving the small joints of hands & feet, classically the interphalangeal joints. May also affect large joints as knee, hip, elbow, wrist, ankle & temporomandibular joints. Usually symmetrical involvement. The involved joints are swollen, painful & stiff. Lesions include:
 - a) **Chronic inflammation of the synovial membrane**: Gross: Swollen redundant synovium showing exaggerated villous projections. Microscopy:
 - Fibrinoid necrosis
 - Increased vascularity
 - Numerous lymphocytes, plasma cells & histiocytes
 - iv) synovial cell hyperplasia
 - osteoclastic activity of underlying bone → bone erosion.
 - b) **Excessive Granulation tissue** is formed. It creeps under the articular cartilage within the eroded bone and also over the articular cartilage and may communicate on both surfaces, thus stimulating fibrous ankylosis. Because of the creeping pattern this granulation tissue is called **Pannus**.
 - c) **Articular cartilage is destroyed** by collagenase and other proteases released in the pannus. This is followed by fibrous or bony ankylosis. The joints appear swollen, spindle shaped and deformed.

2) Extra-articular lesions:

- a) **Rheumatoid nodules**: Mainly develop subcutaneously over bony prominences, commonly around the elbow and measure from 1-2 cm in diameter. Microscopically: An area of fibrinoid necrosis of collagen surrounded by palisading histiocytes.
- b) **Heart lesions**: Rheumatoid nodules affecting the valves and pericardium.

c) **Vascular lesions**: Arteritis and even phlebitis may occur.

d) **Lymphoid hyperplasia** and enlargement of lymph nodes and spleen.

e) **Amyloidosis** may sometimes occur.

FELTY'S SYNDROME: Rheumatoid arthritis in old age accompanied splenomegaly & pancytopenia

STILL'S DISEASE: (Juvenile rheumatoid Arthritis): occurs in patient under 16 years of age with acute onset, high fever, leukocytosis, splenomegaly and skin rash.

OSTEOARTHRITIS (OA)

خشونة المفاصل

DEFINITION: Osteoarthritis (OA) is a common degenerative disease characterized by primary abnormalities in the articular cartilage of weight bearing joints (knee & hip are the most common sites). It is a disease of elderly (females more common than males). When younger patients develop osteoarthritis, it is secondary to a predisposing abnormality in the joint.

TYPES: Primary (95%) & Secondary (5%) types:

- 1) **Primary Osteoarthritis**: It affects old age; possibly as a result of "wear & tear" of the joint.
- 2) **Secondary Osteoarthritis**: It can affect any age due to one or more of the following causes:
 - a) **Chronic joint stress** e.g. due to obesity and occupational strains.
 - b) **Abnormal joint mechanics** e.g. in cases of:
 - Defective nerve supply to a joint (Charcot's joint), e.g. due to spinal cord lesions (tabes dorsalis of syphilis & others)
 - Congenital joint deformities (angulations, malalignment)
 - Acquired joint deformities e.g. post-traumatic or post-inflammatory injury.
 - c) **Systemic disease** (helping factors): as diabetes mellitus and hemochromatosis.

PATHOLOGY: The large weight-bearing joints and spine are the most commonly affected joints. The main pathological lesions include:

1) **Articular cartilage & bone lesions**:

- Degeneration and softening of articular cartilage. The central part of cartilage finally disappears and the underlying bone is exposed.
- Proliferation of the peripheral parts of cartilage occur → cartilaginous lippings. Ossification of these lippings leads to bony projections (osteophytes).
- Separated portions of degenerated cartilage may float freely in the joint (joint mice)
- The underlying bone undergoes progressive eburnation.

2) **The synovium** may show mild chronic inflammation and osteocartilagenous metaplasia.

CHARCOT'S JOINT (neuropathic arthritis): (X)

This is osteoarthritis due to loss of joint sensation caused by some lesions as tabes dorsalis and syringomyelia. Loss of joint sensation predisposes the joint to undue trauma → degenerative changes.

OTHER TYPES OF ARTHRITIS

- b) **PSEUDOGOUT (CHONDROCALCINOSIS)**: It is joint disease characterized by deposition of calcium pyrophosphate. The cause is unknown, occur in old patients and involve the knee joint after trauma or surgery. It is manifested as self-limited acute arthritis.
- c) **GOUTY & TUBERCULOUS ARTHRITIS** see general pathology

PIGMENTED VILLONODULAR SYNOVITIS

inflammatory in nature? HCG + oval

DEFINITION: An uncommon disease characterized by proliferation of synovial membrane of joints, mainly knee. It occurs in adults & is manifested by painful joint swelling & progressive joint disability.

SITES: Knee joint is a common site. Other joints as hip, ankle... etc may be affected.

AETIOLOGY: Unknown, may be of inflammatory nature or a benign neoplastic process.

GROSS: Synovial membrane is thickened and shows villous outgrowths that have a typical orange-brown color due to presence of haemosiderin.

MICROSCOPY: Shows villi covered by proliferating synovial epithelial cells and having vascular connective tissue core infiltrated by large number of foamy histiocytes, histiocytes engulfing haemosiderin, lymphocytes, plasma cells and multinucleated giant cells. Local recurrence may occur, probably due to incomplete synovial removal.

SYNOVIAL SARCOMA (Malignant Synovioma)

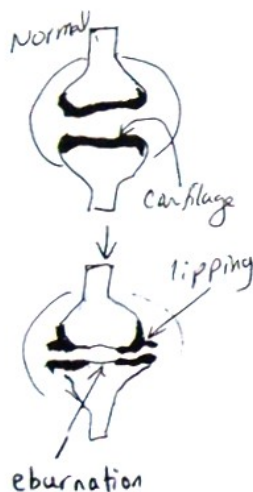
MCC from bursa & tendon sheaths within joints

It is a rare malignant neoplasm arising from synovial epithelial cells. It occurs much more commonly in relation to bursae and tendon sheaths than within joints. Therefore it tends to present as extraarticular soft tissue mass near a joint in the extremities, in particular, the knee and ankle joints.

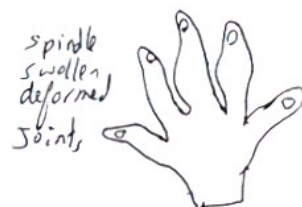
Gross: A grayish lobulated pseudocapsulated mass with areas of necrosis, hemorrhage and cystic degeneration.

Microscopy: Highly cellular neoplasm with a biphasic pattern being composed of spindle cells and epithelium-lined slit-like spaces.

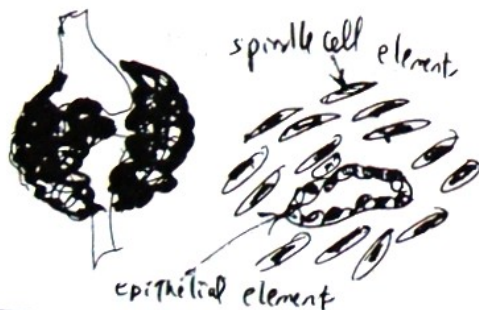
OSTEOARTHRITIS



RHEUMATOID ARTHRITIS



SYNOVIAL SARCOMA



DISEASES OF THE LYMPHOID TISSUE

LYMPHADENITIS

Lymphadenitis is a common.

1- Acute bacterial lymphadenitis:

Aetiology: It affects lymph nodes draining acute infective lesions e.g. cervical lymph nodes in case of acute tonsillitis or tooth infection and mesenteric nodes in case of typhoid fever or acute appendicitis.

Pathology: Enlarged discrete nodes showing congested capillaries, neutrophils and macrophages.

2- Acute viral lymphadenitis

a) Measles.

b) Infectious mononucleosis:

Definition & Aetiology: An infective disease caused by Epstein-Barr virus characterized by fever, sore throat, generalized lymph node enlargement and sometimes splenomegaly.

Pathology:

- Generalized lymph node enlargement.

The affected nodes show striking paracortical blast transformation

- Splenomegaly.

- The peripheral blood shows lymphocytosis with many abnormal T lymphocytes

- Lymphocytic infiltration of liver, brain, meninges may sometimes occur.

- The disease is usually self limiting

3- Acute chlamydial infection in case of lymphogranuloma venereum

4- Chronic nonspecific lymphadenitis

Aetiology: Occurs in lymph nodes draining areas of chronic bacterial infections.

Pathology: The affected nodes are enlarged, firm and discrete. Microscopically they show chronic inflammatory cells associated with reactive follicular hyperplasia (enlarged follicles with reactive prominent germinal centers) and/or sinus histiocytosis.

5- Chronic specific/ granulomatous lymphadenitis e.g.

- Tuberculosis
- Atypical mycobacteriosis.
- Sarcoidosis
- Leprosy
- Syphilis
- Toxoplasmosis.

TUMORS OF LYMPH NODES

1- Secondary Tumors (Metastases):

These are more common than primary tumors & occur in lymph nodes draining a tumor (most commonly carcinoma) e.g. axillary nodes in case of breast cancer & pericolic nodes in case of colorectal cancer. The affected nodes are enlarged, firm with a grayish cut surface. Microscopically they show tumor cell deposits that resemble the primary tumor from which they are derived.

2- Primary Tumors (Lymphomas):

- Lymphomas:** These are also common tumors and are among the most common malignant tumors affecting the human body & are classified into Hodgkin's lymphoma & Non-Hodgkin's lymphoma.
- Others** as angiosarcoma & Kaposi's sarcoma: These are rare tumors.

(A) Enumerate
acute lymphadenitis bacterial
acute viral lymphadenitis
acute chlamydial
chronic non specific
chronic specific
reactive follicular hyperplasia
Painful bec of enlarged non-painful lymph
No BCG

No BCG

more common

LYMPHOMAS

malignant tumor of lymph node
Nodal
extranodal

(A) GENERAL FEATURES OF LYMPHOMAS:

• Patterns of involvement:

- 1-Lymphomas are primary malignant neoplasms of lymphoreticular tissue.
- 2-Lymph nodes are the commonest site (**Nodal Lymphoma**), but the spleen and extranodal sites (tonsils, nasopharynx, GIT, bone marrow, lungs, thyroid, testis, ovary, thymus, skin, salivary glands, brain, ocular adenexa and other organs) are other possible sites of primary lymphoma (**Extranodal Lymphoma**).
- 3-Nodal lymphomas (which are more common than extranodal lymphomas) commonly arise as a localized affection of a group of lymph nodes (most commonly cervical) and may finally lead to generalized lymph node involvement. They may disseminate by blood leading to involvement of **extranodal sites**.
- 4-Nodal lymphomas may sometimes occur as a generalized disease from the start.
- 5-Some types of lymphoma may be associated with or followed by **leukemia**.

• Gross Features: Different types of lymphomas have more or less similar gross features:

- 1- The affected nodes are enlarged, firm with a **homogeneous grayish pink cut section**. The enlarged nodes **are first discrete**, but may become fused due to capsular invasion leading to formation of irregular large fixed mass. *+ Painless * T10*
- 2- Affection of spleen → multiple (usually) grayish nodules → splenomegaly.
- 3- Affection of extranodal sites similarly appears as grayish pink nodules.

• Microscopic Features: Nodal lymphomas are characterized by:

- 1- Loss of nodal architecture.
- 2- Replacement of the node by neoplastic lymphoid cells which infiltrate the subcapsular sinus.

CLASSIFICATION: 1- Hodgkin's Lymphoma. 2- Non- Hodgkin's Lymphoma.

HODGKIN'S LYMPHOMA (HL)

(A) + GIP + VIP

It is a common lymphoma. It occurs at any age. It usually starts in cervical nodes.

GROSS: See above & describe.

MICROSCOPY:

A-Loss Of Nodal Architecture And Replacement Of Nodal Tissue By:

- 1-**Neoplastic Cells:** Their histogenesis (origin) is not yet settled:
 - a) **Reed- Sternberg Cells (RS cells):** These are large cells, 30 - 60 u in diameter with amphophilic cytoplasm and multiple (commonly 2) mirror image nuclei containing large eosinophilic nucleoli.
 - b) **Mononuclear Hodgkin's cell:** It is smaller than RS cell, with a single nucleus having an eosinophilic nucleolus. The cytoplasm is amphophilic.
 - c) **Lacunar cell:** It resembles RS cells but with shrunken cytoplasm that creates a clear space between the shrunken cytoplasm and the cell wall. It is the most common cell in nodular sclerosing type.
 - d) **L & H cells (atypical lymphocyte & histiocytes cells):** These are large mononuclear cells with twisted or lobated nuclei and multiple small nucleoli.
- 2-**Non- Neoplastic (Reactive) Cells:** A variable mixture of lymphocytes, plasma cells, neutrophils, eosinophils and macrophages.
- 3-**Necrosis And Fibrosis:** May occur (see histological types).

B-Histological Classification of HL: Rye's Classification:

- 1-**Nodular lymphocyte predominant type (5%):** It is characterized by nodules of reactive lymphocytes with their central portions showing predominance of L & H cells with no or few RS cells. Prognosis is good. *Good of lymphoma*
- 2-**Lymphocyte rich type (5%):** Characterized by a diffuse background composed of reactive lymphocytes with many mononuclear Hodgkin's cells and very rare RS cells. Good prognosis

- 3- **Nodular sclerosing type (60%):** It is characterized by numerous lacunar cells in addition to RS cells. There are variable reactive cells. Thick bands of collagen, occur and may divide the node into nodules. It has a relatively good prognosis.
- 4- **Mixed cellularity type: (25%)** There are numerous RS cells & Hodgkin's mononuclear cells associated with a mixture of reactive cells (lymphocytes, plasma cells, eosinophils, neutrophils, histiocytes...). This type is more aggressive than the above 2 types.
- 5- **Lymphocyte depletion type: (1- 5%).** It is characterized by very numerous RS cells and mononuclear Hodgkin's cells. Lymphocytes are very few. Necrosis and diffuse fibrosis may occur. Prognosis is poor. Recently there is a trend to classify this type independent of Hodgkin's lymphoma

Remarks:

- 1-Lymphocyte predominant types can (if untreated) change into mixed cellularity or lymphocyte depletion types. Nodular sclerosing type does not change into other types.
- 2-The original Rye's classification did not include nodular lymphocyte predominant type (only recently identified as a separate entity)

CLINICAL FEATURES:

- 1-**Enlarged lymph nodes** and may be **splenomegaly**. *painless*
- 2-**Systemic Manifestations:** Hodgkin's lymphoma may be associated with a) **intermittent fever** (Pel-Ebstein fever) b) **anemia**, c) **night sweats** d) **loss of weight**. The presence of these manifestations indicates a more aggressive disease course.

CLINICAL STAGING OF HL:

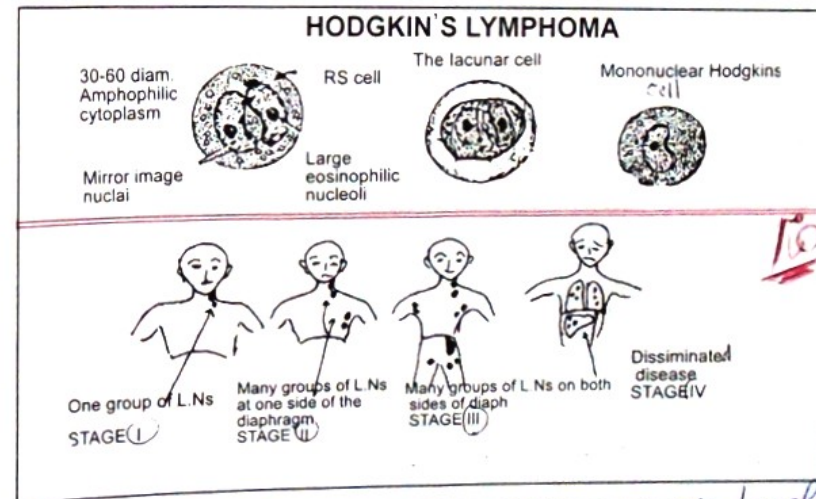
Hodgkin's disease is divided into 4 stages (I, II, III & IV). Each stage is further subdivided according to the presence or absence of systemic manifestations into (A) absent or (B) present. Example Stage III B or III A.

Stage I: The disease is limited to only one group of lymph nodes (e.g. cervical).

Stage II: Two or more groups of nodes but to one side of diaphragm (above or below).

Stage III: Many groups of lymph nodes above and below diaphragm (including spleen)

Stage IV: Affection of non- lymphoid organs due to blood spread.



2) NON - HODGKIN'S LYMPHOMAS (NHL)

May arise in lymph nodes or in extranodal sites. They may be of B or T cell origin (rarely of NK cell or histiocytic origin). Some of these lymphomas are associated with or followed by leukemia. *in lymph or extranodal sites B or T + leukemia*

White blood cells

CLASSIFICATIONS OF NHL

1- THE WORKING FORMULATION CLASSIFICATION OF NHL

According to Working Formulation (WF) lymphomas are classified into low, intermediate and high grades. Nowadays this classification is not popular (does not include many lymphoma types)

LOW GRADE:	INTERMEDIATE GRADE	HIGH GRADE
Small lymphocytic lymphoma/ CLL Plasmacytoid variant. Follicular: predominantly small cleaved cell Follicular: mixed small cleaved and large cell	Follicular: predominantly large cell Diffuse: small cleaved cell Diffuse: small and large cell Diffuse: large cell	Large cell: immunoblastic Lymphoblastic lymphoma. Burkitt's lymphoma

2-KIEL CLASSIFICATION

	B cell lymphomas	T cell lymphomas
LOW GRADE	Lymphocytic: chronic lymphocytic and hairy cell leukemia. Lymphoplasmacytoid Plasmacytic: multiple myeloma. Centroblastic/centrocytic follicular Centroblastic/centrocytic diffuse Centrocytic	Lymphocytic: chronic lymphocytic leukemia Small cerebriform cell: mycosis fungoides and Sezary syndrome Angioimmunoblastic lymphadenopathy Lymphoepithelioid T zone lymphoma Pleomorphic, small cell
HIGH GRADE	Centroblastic Immunoblastic Anaplastic Lymphoblastic Burkitt's lymphoma	Immunoblastic Pleomorphic, medium or large cell Anaplastic Lymphoblastic

3-REAL/WHO CLASSIFICATION (2001)

Precursor cell lymphoma

Lymphoblastic lymphoma: T cell & B cell types.

Peripheral B cell neoplasms

- B-Small lymphocytic lymphoma/ chronic lymphatic leukemia
- B-prolymphocytic leukemia
- Lymphoplasmacytic lymphoma
- Mantle cell lymphoma
- Follicular Lymphoma: Grade 1, 2 & 3
- Extranodal marginal zone B cell lymphoma (MALT lymphoma)
- Nodal marginal zone B cell lymphoma/ monocytoid B cell L
- Splenic marginal zone B cell lymphoma
- Hairy cell leukemia
- Diffuse large B cell lymphoma (including B immunoblastic variant)
- Burkitt's lymphoma (including Burkitt's-like lymphoma).
- Plasmacytoma, plasma cell myeloma

Peripheral T & NK cell neoplasms

- T-prolymphocytic leukemia
- T-cell granular lymphocytic leukemia
- Mycosis fungoides/Sezary syndrome
- Peripheral T cell lymphoma, unspecified
- Angioimmunoblastic T cell lymphoma
- Extranodal NK/T cell lymphoma, nasal & nasal type (angiocentric types)
- Aggressive NK cell leukemia
- Enteropathy type T cell lymphoma
- Hepatosplenic $\gamma\delta$ T cell lymphoma
- Subcutaneous panniculitis-like T cell lymphoma
- Anaplastic large cell lymphoma T/null cell, primary systemic type
- Anaplastic large cell lymphoma T/null cell, primary cutaneous type
- Adult T cell lymphoma/leukemia (HTLV-1+)

LOW GRADE LYMPHOMAS (x) oral

1-Diffuse small lymphocytic lymphoma (SLL):

- It is a B cell lymphoma that occurs in elderly adults and many cases are associated with chronic lymphatic leukemia (CLL)
- As with many other lymphomas, generalized lymph node affection & hepatosplenomegaly are common.
- Microscopy: Diffuse effacement of lymph node architecture by well differentiated small lymphocytes that show dark nuclei, inconspicuous nucleoli and rare mitoses.
- May undergo transformation into large cell lymphoma (Richter's transformation)
- Positive for B cell markers as CD20

2-Diffuse small lymphocytic lymphoma with plasmacytoid differentiation:

It is a small B cell lymphoma like SLL + plasmacytoid cells (cells with eccentric nuclei)

3-Follicular lymphoma (FL): Low & higher grade variants:

- A lymphoma of B cells, arising from the follicular center cells (FCC), mainly adults.
- Neoplastic lymphocytes are grouped into follicles.
- May be totally follicular or have diffuse areas
- The neoplastic follicles consist of a mixture of :
 - Small cleaved lymphocytes (centrocytes) = small lymphocytes with cleaved nuclei
 - large non-cleaved cells (centroblasts).
- Follicular lymphoma is graded according to frequency of centrocytes & centroblasts:
 - Grade 1 (low grade): Centrocytes + 1-5 centroblasts/ hpf
 - Grade 2 (intermediate grade): Centrocytes + 6-15 centroblasts/ hpf
 - Grade 3 (high grade): Centrocytes + > 16 centroblasts/ hpf
- As with many other lymphomas, generalized lymph node & spleen involvement are common
- May progress to diffuse lymphoma.
- It is very important microscopically to differentiate between neoplastic follicles of FL and hyperplastic follicles of stimulated lymph nodes, since the later are benign.

Neoplastic follicles of FL

- Follicles have no germinal centers
- Cells are monoclonal (detected by immunohistochemistry)
- Cells express Bcl2 marker

Hyperplastic follicles

- Follicles have germinal centers
- Cells are polyclonal
- Cells are negative for Bcl2

4-Mantle cell lymphoma:

- It arises from B lymphocytes at the mantle cell zone (at periphery of the lymphoid follicles).
- Histologically low grade, but some cases are biologically aggressive
- It consists of small and medium-sized lymphocytes that may resemble centrocytes, but express different markers, as cyclin D1 & CD5
- May undergo transformation into large cell lymphoma

5-Marginal zone lymphoma:

- It may be extranodal arising from mucosa associated lymphoid tissue (MALT) as in case of lymphocytic gastritis. MALT lymphoma is low grade but may undergo large cell transformation (high grade)
- It may be nodal arising from the marginal zone next to Mantle zone. May also $\rightarrow$ large cell lymphoma

6-Low grade T cell lymphomas: There are many types as mycosis fungoides (low grade skin lymphoma) & others. T cell lymphomas express T cell markers as CD3, CD4 & CD8

HIGH GRADE LYMPHOMAS (x) oral

1-Diffuse Large B cell lymphoma: Consists of large B lymphocytes that have large nuclei with frequent prominent nucleoli and mitotic figures

2- Large cell immunoblastic lymphoma: It is also a large cell lymphoma of B or T cell origin, mainly affecting adults. It consists of a diffuse population of large immunoblastic cells showing large nuclei with two prominent nucleoli and very high mitotic activity.

3-Anaplastic large cell lymphoma (ALCL)

- It consists of large extremely anaplastic lymphocytes that express CD30 marker
- May be of T cell or B cell origin
- May affect the skin (cutaneous ALCL), usually children, favorable prognosis
- Affects LNs, mainly adults, aggressive

4-Lymphoblastic Lymphoma :

- It is of either B or T cell origin. It affects children and adolescents as well as adults
- Commonly affects mediastinal lymph nodes with frequent hepatosplenomegaly
- It is a diffuse lymphoma composed of lymphoblasts which appear slightly larger than normal lymphocytes and show dusty chromatin, inconspicuous nucleoli and high mitotic activity with frequent admixture of non-neoplastic pale staining macrophages giving the tumor a "starry sky" appearance. Cells are positive for CD99

3- Burkitt and Burkitt-like lymphoma: Small noncleaved cell lymphoma:

- **Burkitt's lymphoma** is a B cell lymphoma that mainly affects African children due to Epstein Barr virus infection. It is one of the most aggressive human neoplasms with the tumor doubling time only 24-48 hours. It commonly affects the jaws, lymph nodes, gonads, GIT and other sites. It consists of a diffuse population of small lymphocytes with round nuclei showing two or more nucleoli and very high mitotic activity and a striking starry sky appearance (the sky pattern being represented by the darkly stained compact population of lymphocytes, while the starry pattern is given by the scattered pale stained macrophages).
- **Burkitt-like lymphoma** is also an aggressive B cell lymphoma that closely resembles Burkitt's lymphoma, but has different anatomical distribution and tends to occur in adults.

CAUSES OF SPLENOMEGALY

1-Infectious:

- Bacterial: As T.B., typhoid and septicaemia (acute splenic swelling).
- Viral: Infectious mononucleosis.
- Parasitic: As bilharziasis, malaria, kala-azar, hydatid cysts...

2-Vascular Disorders:

- Portal hypertension due to cirrhosis or hepatic bilharziasis.
- Chronic venous congestion due to right-side heart failure.
- Recent infarcts.

3-Blood diseases:

- Leukaemia
- Haemolytic anaemias
- Polycythaemia vera
- Thrombocytopenia.

4-Tumors:

- Malignant:**
 - Primary tumors as lymphomas, and rarely angiosarcoma or Kaposi's sarcoma
 - Secondary tumors (metastasis) unlike lymph nodes, they are rare in the spleen
- Benign** as lymphangioma, hemangioma & fibroma.

5-Metabolic disturbances as amyloidosis, haemochromatosis and lipid storage diseases.

6-Hypersplenism:

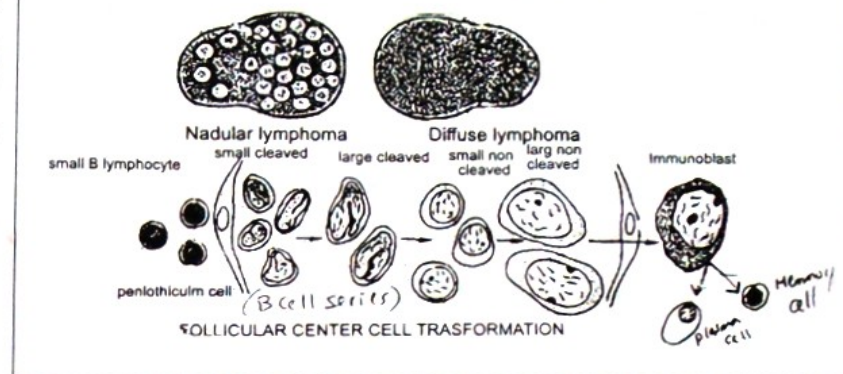
Definition & Effects: This is splenic enlargement associated with increased destructive activity to blood cells leading to pancytopenia (anaemia, leucopenia and thrombocytopenia).

Types & Causes: There are 2 types:

- Primary Hypersplenism:** Rare. Unknown cause.
- Secondary Hypersplenism:** Occurs in cases of splenomegaly due to a known cause e.g.
 - Infections as Bilharziasis, malaria
 - Chronic venous congestion
 - Lymphomas & leukemias
 - Lipid storage diseases...
 - Rheumatoid arthritis

Handwritten notes:
 * Congenital & metabolic
 * Traumatic injuries
 * Infectious
 T.B. & leishmaniasis
 acute splenic swelling
 infectious mononucleosis
 * Neoplastic (lymphoma)
 * Vascular portal hypertension
 Reactions

NON-HODGKIN'S LYMPHOMA



CAUSES OF LYMPH NODE ENLARGEMENT

- 1) Acute or chronic lymphadenitis (enumerate)
- 2) Reactive lymph node hyperplasia
- 3) Lymph node tumors:
 - a) Primary = Lymphoma
 - b) Secondary: Metastases
- 4) Blood diseases: mainly leukemia
- 5) Some metabolic storage diseases

Handwritten notes:
 = Leishmaniasis
 Same as splenomegaly with no vascular causes

THE NORMAL DIFFERENTIATION OF B & T CELLS

To understand cell types of lymphoma according to recent classifications, the normal differentiation of B and T lymphocytes must be understood.

B LYMPHOCYTE DIFFERENTIATION

- Precursor Lymphoid stem cell → B lymphoblast (in bone marrow) → B prolymphocyte → B lymphocyte (naïve or virgin **small B cells**) → Peripheral blood (10-20% of lymphocytes) → Homing (lymph nodes, spleen & other areas)
- In lymph nodes: Naïve B cells (1° follicles) → Antigen Stimulation → **Germinal center (GC) cells** which may be small noncleaved or cleaved (centrocytes) or large (centroblasts). Centrocytes → Plasma cells + Marginal B cells, of which some are memory cells. -Non GC cells (**immunoblasts**, plasmablasts) → plasmacytoid cells and plasma cells.
- Now this is a 2° follicle. What remains of naïve cells at the periphery is the mantle zone.

T LYMPHOCYTE DIFFERENTIATION

- Precursor Lymphoid stem cell → T lymphoblast (thymus) → T prolymphocyte → T lymphocyte → Peripheral blood (60-70% of lymphocytes) → Homing (resting T lymphocytes in LNs, spleen & other areas)
- Resting T lymphocytes → Antigen Stimulation → Blasts (**lymphoblasts/immunoblasts**) → clonal proliferation & maturation → Sensitized T cells (lymphokine secreting) & memory T cells.

HEMATOPOIETIC & HEMATOLOGICAL DISORDERS

Hematopoietic (bone marrow) and hematological (peripheral blood) disorders include:

DISEASES OF LEUKOCYTES

LEUKEMIA (B) *normal + KCG*

DEFINITION AND GENERAL PATHOLOGICAL FEATURES:

Leukemia is a serious condition characterized by:

- Neoplastic proliferation of the leukocyte forming tissues (bone marrow + lymphoid tissue).
- Blood changes: 1) Invasion of blood by a large number of neoplastic leucocytes which may be immature (blasts) in case of acute leukemia or mature in case of chronic leukemia. 2) Anemia due to defective red cell production (myelophthysic anemia). 3) Thrombocytopenia due to defective platelet production. This leads to increased bleeding tendency.
- Hepatomegaly due to leukemic infiltrates
- Splenomegaly due to leukemic infiltrates. Infarcts are common due to thrombosis.
- Generalized lymph node enlargement (due to leukemic involvement) is common.
- Leukemic infiltrates of other organs as brain and kidney...
- Leukemia may be acute (fatal within 6 months) or chronic (fatal within 1-10 years)
- Secondary changes:
1) Lowered immunity; thus infections are common.
2) Gout in case of chronic myeloid leukemia due to excess production of uric acid

AETIOLOGY:

- Irradiation, virus and chemical as benzol and aniline dyes are important factors.
- Genetic abnormalities: The Philadelphia chromosome (a hybrid chromosome resulting from reciprocal translocations between chromosomes 9 & 22) is detected in some types of myeloid leukemia.

CLASSIFICATION:

- 1- Acute Leukemia: a) Myeloid type b) Lymphatic type.
- 2- Chronic Leukemia: a) Myeloid type b) Lymphatic type.
- 3- Rare types of leukemia: a) Hairy cell leukemia b) Histiocytic leukemia c) Stem cell leukemia d) Erythroleukemia (erythromyeloblastic leukemia, DiGuglielmo's disease) e) Plasma cell leukemia

ACUTE LEUKEMIA

- Characterized by an abrupt onset. Course of untreated cases is rapidly fatal (6 months)
- Blood analysis: A high white blood cell count (usually less than 50,000 but may be up to 100,000 or more / cmm). Most of the cells are blast cells (myeloblasts or lymphoblasts).
- The clinical presentation includes fatigue (due to anemia), fever, bleeding, bone pain and tenderness, in addition to hepatosplenomegaly and generalized lymph node enlargement.
- The two major types of acute leukemia include:

1- Acute lymphoblastic leukemia (ALL):

It mainly affects children. Lymphoblasts cannot be easily distinguished from myeloblasts. However special laboratory techniques can help in differentiation, e.g. lymphoblasts are positive for acid phosphatase while myeloblasts are positive for peroxidase. Recently ALL was subclassified into L1 (small cell), L3 (large cell) & L2 (combined features of L1 & L2).

2- Acute myeloblastic leukemia (AML): It mainly occurs in adults.

Recently AML was classified into several subtypes according to the French - American - British (FAB) Classification. This is of important therapeutic and prognostic value.

THE FAB CLASSIFICATION OF AML:

CLASS	MORPHOLOGY
M1: Acute myelocytic leukemia without differentiation.	Myeloblasts predominate.
M2: Acute myelocytic leukemia with differentiation.	Myeloblasts + promyelocytes.
M3: Acute promyelocytic leukemia.	Promyelocytes.
M4: Acute myelomonocytic leukemia.	Resembles M2 + Monocytic differentiation
M5: Acute monocytic leukemia.	Promonocytes and/or blasts
M6: Acute erythroleukemia.	Myeloblasts + megaloblastoid erythrocytes
M7: Acute megakaryocytic leukemia	Undifferentiated blasts that react with antiplatelet antibodies

CHRONIC LEUKEMIA

Characterized by gradual onset and long course up to several years. Blood analysis reveals a high leucocytic count. The cells of chronic leukemia are mature. Two major types of chronic leukemia:

1) Chronic myeloid leukemia (CML):

- Age of patients: 25-60 years.
- Bone marrow: Hypercellularity with increased myeloid cells (granulocytes including eosinophils).
- Peripheral blood: The total leucocytic count rises to 75,000-250,000. Most of the cells are mature granulocytes and late myelocytes.
- Hepatomegaly, splenomegaly and generalized lymph node enlargement.
- Other organs may show leukemic infiltrates.
- Gout is a common sequel (in addition to other complications mentioned before).

2) Chronic lymphocytic leukemia (CLL): This is the commonest leukemia.

- Age of patients: old persons over the age of 50 years.
- Bone marrow shows scattered foci of small mature lymphocytes in an otherwise normal background.
- Generalized lymph node enlargement. The lymph nodes show the picture of diffuse small lymphocytic lymphoma.
- Peripheral blood: lymphocyte count is up to 100,000. Most cells are mature lymphocytes.
- Hepatomegaly, splenomegaly...
- Other organs show leukemic infiltrates.
- Autoimmune hemolytic anemia is common (+ the other complications mentioned before).

OTHER DISORDERS OF LEUKOCYTES

LEUCOCYTOSIS:

- Non-leukemic increase of the leucocytic count above normal (above 10,000 / cmm) is mainly due to increase of neutrophils (neutrophilic leucocytosis) as in pyogenic infections.
- Subtypes of leucocytosis include eosinophilia (observed in cases of hypersensitivity as bronchial asthma, urticaria and parasitic infections), monocytosis (as in typhoid and infectious mononucleosis) and lymphocytosis (as in viral and tuberculous infections)

LEUCOPENIA:

- This is decrease of leucocytic count below 4000 / cmm.
- It may be due to a) Bone marrow hypofunction as in cases of bone marrow aplasia, severe toxemia and vitamin B12 or folic acid deficiency b) Hypersplenism.

AGRANULOCYTOSIS:

A severe form of leucopenia with a total leucocytic count less than 1000 / cmm. It is predominantly due to marked neutropenia. It has the same causes of leucopenia. There is marked lowering of immunity resulting in severe inflammatory necrotizing lesions e.g. agranulocytic angina of mouth.

DISORDERS OF LEUKOCYTE FUNCTION e.g. defective neutrophil phagocytosis.

DISEASES OF RED BLOOD CELLS

POLYCYTHEMIA

Increase of blood erythrocytes (polycythaemia) may be :

- a) **Secondary** (reactive) type due to bone marrow stimulation in cases of hypoxia (high altitudes, chronic lung diseases, congenital cyanotic heart diseases)
- b) **Primary** type (polycythemia Vera): A serious neoplastic disease of bone marrow. There is marked increase of peripheral RBCs leading to marked increase of blood viscosity. Thrombosis is common, leading to infarctions. Splenomegaly occurs.

ANEMIA

DEFINITION: Anemia is a decrease of peripheral red blood cell count i.e reduction of hemoglobin concentration and hence reduction of the oxygen transport capacity of the blood.

GENERAL PATHOLOGICAL FEATURES OF ANEMIA:

1-Peripheral blood:

- a) Decreased red blood cell count (below 5,000,000 per cmm for adult male)
- b) RBCs may be microcytic (iron deficiency anemia), macrocytic (megaloblastic anemia) or normocytic.
- c) According to hemoglobin concentration per red cell anemia may be normochromic or hypochromic
- d) According to type of anemia, abnormal red cells may be seen e.g spherocytes or immature forms

2-Bone marrow pathology:

- a) Hyperplasia in some types of anemia
- b) Aplasia (in aplastic anemia) or destruction by tumors (in myelophthisic anemias)
- 3- **Extramedullary hemopoiesis** occurs in liver, spleen, & lymph nodes in some types of anemia
- 4- **Tissue changes:**
 - a) Pallor of skin & mucus membranes.
 - b) Hypoxic fatty change of parenchymal cells as liver, myocardium & kidney.

AETIOLOGICAL CLASSIFICATION OF ANEMIAS:

1- **Blood loss:** acute (post hemorrhagic anemia) or chronic.

2- **Excessive red cell destruction** (hemolytic anemias):

- a- Intracorporeal causes: as spherocytosis, thalassemia, sickle cell anemia and enzyme deficiencies.
- b- Extra corporeal causes as septicemia, malaria, lead poisoning, some drugs, autoimmunity and trauma (e.g. cardiac traumatic hemolytic anemia).

3- **Impaired red cell production:**

- a- Due to **Bone marrow hypofunction:** aplastic anemia, renal failure & endocrine disorders & bone marrow destruction by tumors (myelophthisic anemia).
- b- **Deficiency anemias:** e.g. iron deficiency, B12 deficiency and folic acid

ACUTE POST HEMORRHAGIC ANEMIA

It follows loss of large amounts of blood (traumatic Hge, perforated peptic ulcers, ruptured varices...etc). It is a normocytic anemia. Compensatory bone marrow hyperplasia occurs and the peripheral blood shows reticulocytosis, leukocytosis and thrombocytosis.

HEMOLYTIC ANEMIAS

Aetiology:

1) **Congenital causes** as spherocytosis, sickle cell anemia, thalassemia & favism.

Spherocytosis: An autosomal dominant disease characterized by defective red cell membranes. The red cells are easily destroyed and hemolysed.

Sickle cell anemia: A hereditary disease characterized by structural abnormality of hemoglobin (Hb S). Sickling of RBCs occurs when oxygen is reduced → destruction & hemolysis of RBCs

Thalassemia (Cooley's anemia, Mediterranean anemia) : Another hereditary disease with abnormal hemoglobin type (Hb F). RBCs are fragile & become easily destroyed & hemolysed.

2) **Acquired causes** as

- a) **Rh incompatibility (erythroblastosis fetalis):** When an Rh positive male marries an Rh negative female, the RBCs of an Rh positive fetus may be destroyed by antibodies produced in his mother. This may result in:
 - Still birth due to marked hemolysis.
 - Infant is borne alive and develops hemolytic anemia and hemolytic jaundice (icterus gravis neonatorum), basal ganglia destruction (kernicterus) marked oedema and ascites (hydrops fetalis). The infant dies within few weeks.
- b) **Infections** as malaria & septicemia
- c) **drugs & chemicals** as arsenic and phosphorus.

Pathology:

- Normocytic normochromic anemia, associated with reticulocytosis, leukocytosis & thrombocytosis.
- Bone marrow hyperplasia
- Extramedullary hemopoiesis in liver, spleen & lymph nodes.
- Hepatomegaly & splenomegaly due to a) extramedullary hemopoiesis b) Hyperplasia of reticuloendothelial cells.
- Generalized hemosiderosis. Hemolytic anemia. Gall bladder pigment stones.

IRON DEFICIENCY ANEMIA

Aetiology:

- 1- Dietary deficiency of iron
- 2- Chronic hemorrhage (e.g bilharziasis)
- 3- Ankylostomiasis
- 4- Malabsorption

Pathology:

- 1- Microcytic hypochromic anemia
- 2- Bone marrow hyperplasia
- 3- Atrophic epithelial changes e.g atrophy of gastric mucosa (leading to hypochlorhydria), atrophy of buccal mucosa, atrophy of vaginal mucosa, spooning of nails.

MACROCYTIC ANEMIAS

Aetiology:

- 1- Deficiency of extrinsic factors : vitamin B12 or folic acid.
- 2- Deficiency of intrinsic factor which is produced by gastric mucosa & is deficient in case of pernicious anemia.

Pathology:

- 1- Macrocytic anemia, associated with leucopenia and thrombocytopenia.
- 2- Bone marrow hyperplasia (megaloblastic)

Types:

- 1- **Pernicious anemia:** An autoimmune disease characterized by:
 - a) Atrophic gastritis with deficient production of intrinsic factor. Gastric carcinoma is a complication.
 - b) Subacute combined degeneration of the spinal cord in up to 10% of cases
 - c) Hemosiderosis may occur due to impaired utilization of iron by the bone marrow.
- 2- **Macrocytic anemia of pregnancy:** Rare. Due to deficiency of folic acid & B12.
- 3- **Others:** a) In case of malabsorption syndromes b) following gastrectomy.

ANEMIAS DUE TO BONE MARROW HYPOFUNCTION

1- **Aplastic Anemia:**

Aetiology: Bone marrow aplasia may be

- a) Primary (idiopathic).
- b) Secondary caused by bone marrow irradiations or drug toxicity (e.g chloramphenicol).

Pathology:

- a) Normocytic anemia associated with leucopenia and thrombocytopenia
- b) Bone marrow is hypocellular and consists of fibrofatty tissue
- c) Spleen is atrophic
- d) Generalized hemosiderosis due to impaired utilization of iron by the bone marrow.
- e) Extramedullary hemopoiesis: Uncommon

2-Myelophthisic Anemia: Normocytic anemia due to bone marrow destruction by tumors

THE PATHOLOGICAL FEATURES OF SOME COMMON FORMS OF ANEMIA

are summarized in the following table:

Type of Anemia Features	Post-Hemorrhagic	Haemolytic	Iron Deficiency	Macrocytic	Bone marrow hypofunction
*Peripheral blood R.B.Cs W.B.Cs & Platelets	Normocytes Increased	Normocytes Increased	Microcytes Normal	Macrocytes Decreased	Normocytes Decreased
*B.M. Hyperplasia *Extramedullary hemopoiesis	Normoblastic type	Normoblastic Common	Normoblastic -----	Megaloblastic may occur	Absent Uncommon
*Splenomegaly *Haemosiderosis	-----	Common Common	Rare (Unexplained) -----	May occur May occur	May be atrophic May occur
*General effects	Pallor, Hypoxia, degeneration of parenchymatous organs; in all types of anaemia				
*Others		Jaundice Gall stones	Epith. Atrophy Nail spooning	Subacute comp. deg. of spinal cord in case of pernicious type.	
*Aetiology	Acute Hge.	Congenital causes as spherocytosis Acquired causes as drugs, septicemia	Dietary deficiency Chronic hemorrhage	Deficiency of extrinsic factors as B12 or folic acid Deficiency of intrinsic factor	Aplastic anaemia may be idiopathic or due to drugs or irradiation.

REMARKS:

- 1-Haemosiderosis in case of macrocytic anaemia and bone marrow hypofunction is due to excess iron unutilized by bone marrow.
- 2-Anaemia due to bone marrow hypofunction includes 1)Aplastic anaemia 2)Myelophthisic anaemia due to replacement of B.M by malignant neoplasm. 3)Anaemia due to toxic depression of B.M.
- 3-Pernicious anaemia is an autoimmune anaemia characterized by deficiency of intrinsic factor, atrophic gastritis and high incidence of gastric carcinoma.

DISORDERS OF PLATELETS**THROMBOCYTOPENIA:**

This is reduced peripheral blood platelet count. It may be :

- 1-**Primary idiopathic (autoimmune) type** which mainly occurs in children and is characterized by spontaneous petechial hemorrhages anywhere in the body. There is also splenomegaly. Bleeding time is prolonged.
- 2-**Secondary type** due to decreased platelet production (due to bone marrow aplasia, vitamin B12 or folic acid deficiency) or increased platelet destruction (hypersplenism).

THROMBOCYTHEMIA:

This is peripheral thrombocytosis .It may be primary (idiopathic) or secondary (as in M7 AML)

COAGULATION DEFICIENCY DISEASES**HEMOPHILIA:**

A sex-linked inherited disease affecting males characterized by deficiency of coagulation factor VIII (antihemophilic globulin).It is characterized by hemorrhages in different organs occurring spontaneously or following trauma (e.g joint hemorrhage = hemarthrosis).Coagulation time is prolonged ,while bleeding time is normal.

OTHERS:

- a) Christmas disease (hemophilia B)
- b) Afibrinogenemia which may be 1) congenital 2)acquired as in cases of DIC.
- c)Vitamin K deficiency.

HAEMORRHAGIC BLOOD DISEASES

Blood diseases with increased tendency to bleed include:

- 1)Thrombocytopenia
- 2)Coagulation Deficiency diseases (see above)
- 3)Others as vitamin C deficiency, toxemia ,septicemia

MYELOPROLIFERATIVE DISORDERS

These are disorders of the myeloid stem cells including:

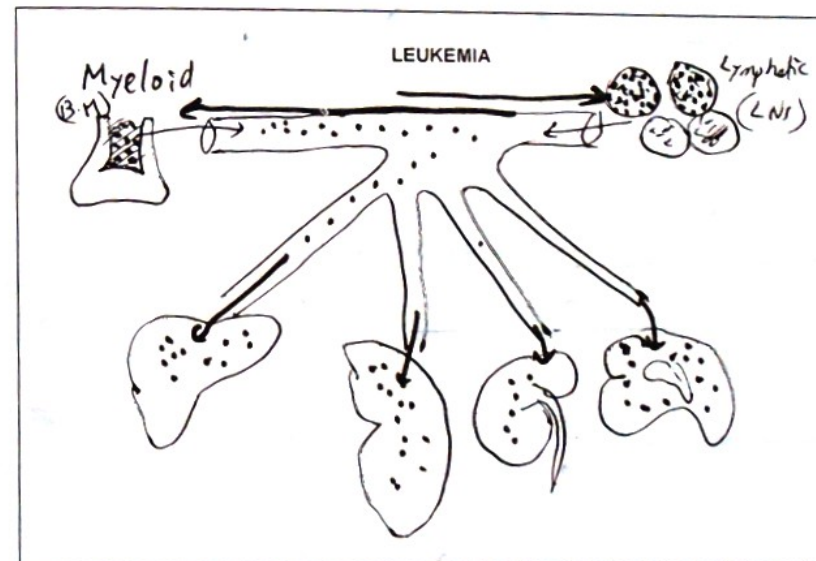
- a)Myeloid leukemia
- b) Polycythemia vera
- c) Myeloid metaplasia with myelofibrosis.

MYELOYDYSPLASTIC SYNDROMES

A group of stem cell disorders characterized by maturation defects resulting in defective hematopoiesis and an increased risk of transformation to acute myeloblastic leukemias.

PLASMA CELL DYSCRASIAS

Abnormal plasma cell proliferation and secretions include multiple myeloma, plasmacytoma, heavy chain disease and primary amyloidosis.



DISEASES OF THE ENDOCRINE GLANDS

THYROID GLAND

Diseases of the thyroid gland are generally more common in females.

THYROIDITIS

1-Hashimoto's Thyroiditis:

Aetiology: Autoimmune. The most likely mechanism of thyroid cell destruction is by cytotoxic T cell-mediated hypersensitivity reaction.

Gross: Symmetrically enlarged, firm rubbery gland. The normal red brown colour of the gland is replaced by pale greyish white appearance.

Microscopy:

1-Extensive replacement of the thyroid by lymphocytes which may sometimes form follicles.
2-Marked atrophy of the follicular epithelium. The residual follicular cells are commonly transformed into large pink cells (Askanazy or Hurthle cells).

Complications:

- 1-Myxoedema.
- 2-Lymphoma (B cell type).

3-Hashi Toxicosis

2-Riedel's Thyroiditis:

Aetiology: Idiopathic.

Gross: Enlarged, adherent, stony hard, greyish thyroid.

Microscopy: Inflammatory fibrosclerosis:

- 1-Patchy chronic inflammatory cell infiltrates associated with:
- 2-Patchy dense fibrosis and hyalinosis.

Complications:

- 1-Myxoedema.
- 2-Severe pressure symptoms.

3-Granulomatous (Subacute or de Quervain's) Thyroiditis:

Aetiology: Unknown, but a viral aetiology is considered most likely.

Gross: Enlarged non-adherent firm greyish thyroid.

Microscopy: Numerous granulomas rich in foreign body giant cells with extensive destruction and fibrosis of thyroid follicles.

Effects: Mild myxoedema.

4-Acute thyroiditis This is suppurative inflammation (abscess) caused by pyogenic bacteria

5-Other Types Tuberculous, syphilitic & fungal thyroiditis.

GOITER

DEFINITION: Enlargement of thyroid gland not due to inflammation or tumors.

TYPES:

- 1-Simple goiter (non-toxic goiter): a) Diffuse b) Nodular
- 2-Toxic goiter: a) Primary type (Grave's disease, exophthalmic goiter). b) Secondary type

1-SIMPLE GOITER

Definition: This is goiter, unaccompanied by thyroid hyperfunction (non toxic goiter)

Aetiology: Iodine deficiency which may be:

- 1-Absolute deficiency (Endemic type):

absolute
relative (high demand)

physiological goitre is various neck

جهاز الغدة - عنق

- Occurs in parts of the world deficient in iodine (e.g Egyptian Oasis). The use of iodinated salt in these areas has markedly reduced the incidence of goiter.
- Regular consumption of goitrogenic substances is another possible factor. Examples of goitrogens include calcium and fluorides in the water supply and thiocyanates in food (Cabbage, cauliflower...).

2-Relative deficiency (Sporadic type): affecting females because of their high iodine demand (due to iodine loss in menses and during pregnancy and lactation).

Pathology:

1-Diffuse Goiter: (Parenchymatous Goiter, Colloid Goiter)

Aetiology and pathogenesis:

- Iodine deficiency → decrease in the output of thyroid hormones → rise of TSH → diffuse thyroid hyperplasia → thyroid enlargement (and rise of hormone output).
- Early enlargement may be called **parenchymatous goiter**, but with persistent iodine deficiency, thyroid is considerably enlarged due to colloid distention of thyroid follicles and this is called **colloid goiter**.

Gross: There is diffuse symmetrical thyroid enlargement. Cut section shows:

- In parenchymatous goiter: Fleshy grayish pink appearance.
- In colloid goiter: Microcystic spaces filled with brownish gelatinous colloid.

Microscopy:

- In parenchymatous goiter: Mildly enlarged thyroid follicles, filled with little colloid & lined by hyperplastic cuboidal epithelium.
- In colloid goiter: Markedly enlarged follicles, distended with abundant colloid & lined by flattened epithelium.

2-Nodular Goiter:

Aetiology and pathogenesis:

Nodular goiter may develop on top of diffuse goiter but the exact pathogenesis is unclear. It is believed that nodular goiter is due to repeated cycles of iodine deficiency (thyroid hyperplasia) and iodine correction (thyroid involution) which create an abnormal gland rhythm accompanied by irregular vascularity, irregular hyperplasia and irregular fibrosis leading to formation of one or commonly multiple nodules (multinodular goiter).

Gross:

- Asymmetrically enlarged thyroid.
- The outer surface and cut section are multinodular. The nodules are variable-sized and separated by fibrous tissue. Some nodules are firm, others show a gelatinous colloid pattern. Secondary changes are common including cystic changes, hemorrhage and dystrophic calcification.

Microscopy: The thyroid follicles within the nodules are very variable reflecting the abnormal gland rhythm; some follicles appear normal, others are hyperplastic or colloid-distended. Cystic follicles are common and may show hyperplastic papillary epithelial projections. Hemorrhage and calcification are common. The nodules are separated by fibrous tissue infiltrated by lymphocytes.

Complications:

- a) Pressure effects.
- b) Retrosternal extension.
- c) Toxic transformation (secondary or toxic nodular goiter).
- d) Malignant change is questionable.

2-GRAVE'S DISEASE

(Diffuse toxic goiter or Exophthalmic goiter)

Pathogenesis:

- Grave's disease is an autoimmune disease characterized by hyperthyroidism associated with exophthalmos. It was formerly believed to be due to the presence of an autoantibody termed LATS (long acting thyroid stimulator). Nowadays, it is believed to be caused by a complex group of autoantibodies, the most important of which are:

due to aut Antibody: LATS
TSH
TGI

Hyperthyroidism
exophthalmos

White tongue

- 1-Thyroid stimulating immunoglobulins (TSI): They act on TSH receptors mimicking the action of TSH.
- 2-Thyroid growth stimulating immunoglobulins (TGI): These initiate the growth of thyrocytes. The mechanism of exophthalmos is obscure. However it was found that TSI has a fibroblast stimulating action and it is thought that it stimulates the fibroblastic proliferation of the retro-orbital tissues leading to exophthalmos.

Pathological features:

A-Pathology of the thyroid gland

Gross: Moderate diffuse symmetrical thyroid enlargement.
The cut section is pink due to high vascularity.

Microscopy:

- 1-Thyroid Follicles:
 - a) The follicles are hyperplastic, their lining is tall columnar with frequent papillary formation.
 - b) They contain small amount of colloid which is peripherally scalloped (vacuolated). This is due to rapid absorption of thyroid hormones.
- 2-Thyroid Stroma shows:
 - a) Excess vascularity.
 - b) Lymphocytic infiltrates.

B-Other pathological features

- 1-Exophthalmos: protrusion of eyeballs with risk of ocular infection and blindness.
- 2-Loss of weight.
- 3-Tremors.
- 4-Left ventricular hypertrophy, tachycardia....
- 5-Pretibial myxoedema occur in 5% of patients due to localized accumulation of mucopolysaccharides forming circumscribed patches in the pretibial skin.
- 6-Diffuse lymphoid hyperplasia of lymphoid organs as thymus and spleen.
- 7-Blood: relative lymphocytosis and may be neutropenia.

Remark: Causes Of Thyrotoxicosis (Hyperthyroidism):

- 1-Grave's disease.
- 2-Toxic nodular goiter.
- 3-Toxic adenoma.
- 4-Hashitoxicosis (a combination of Grave's disease and Hashimoto's disease)

BENIGN TUMORS (ADENOMA)

GROSS: A solitary round encapsulated nodule up to 5 cm. in diameter. Cut section is fleshy grayish pink. Secondary changes including hemorrhage, fibrosis, calcification and cystic changes are common.

MICROSCOPY:

1-Follicular Adenoma:

- Many histological types:
 - a) **Normofollicular** adenoma: composed of normal-sized follicles.
 - b) **Macrofollicular** adenoma (colloid adenoma): composed of large-sized follicles distended with colloid.
 - c) **Microfollicular** adenoma (fetal or embryonal adenoma) composed of very small follicles.
 - d) **Hurthle cell adenoma**: composed of follicles lined by large polyhedral eosinophilic cells having abundant pink granular cytoplasm (Hurthle cells).
- All follicular adenomas are surrounded by a complete fibrous capsule of varying thickness and the normal thyroid parenchyma around the adenoma is compressed. The capsule is intact and there is no vascular invasion. Absence of capsular and vascular invasions is the criterion used to differentiate follicular adenoma from well differentiated follicular carcinoma.

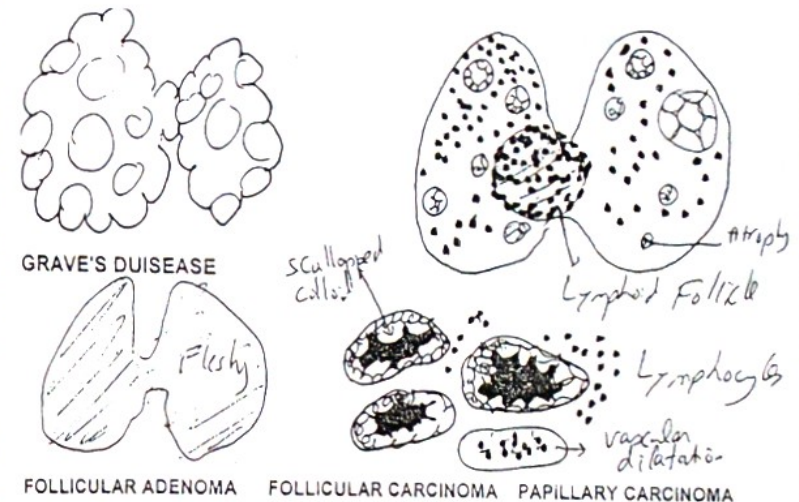
- 2-**Atypical adenoma:** Shows cellular pleomorphism and atypia (but with no vascular invasion)

EFFECTS & COMPLICATIONS:

- 1-Pressure effects.
- 2-Toxic change (toxic adenoma).
- 3-Malignancy.

NODULAR GOITER

HASHIMOTO'S THYROIDITIS



FOLLICULAR ADENOMA

FOLLICULAR CARCINOMA

PAPILLARY CARCINOMA

THYROID CARCINOMA

SEX & AGE: More common in females. Most tumors arise in elderly (above the age of 50 years), but papillary carcinoma may also arise in children & young adults before the age of 20 years.

PREDISPOSING FACTORS:

- 1-Ionizing radiation.
- 2-Thyroid adenoma.
- 3-Nodular goiter: uncertain.

GROSS:

- A greyish irregular firm infiltrating growth which may exceed 10 cm. in diameter
- May also occur in the form of a small or large circumscribed nodule or multicentric nodules.
- Although malignant, some tumors are encapsulated.
- Areas of hemorrhage, necrosis, cystic changes and calcifications may occur.

PATHOLOGICAL TYPES:

1-Papillary carcinoma (best prognosis):

- May arise at any age including children and young adults.
- The malignant cells form cystic spaces showing papillary projections, lined by malignant cells that characteristically show optically clear nuclei with prominent nuclear grooves. The tumor is frequently associated with calcified bodies (psammoma bodies).
- Distant spread is mainly by lymphatics. Blood spread is very rare & late.
- The tumor has the best prognosis among all types of thyroid carcinoma.

2-Follicular carcinoma:

- Usually arises in elderly individuals.
- It is characterized microscopically by follicles (acini) lined by malignant cells, showing dark nuclei. Mitoses are mainly detected in less differentiated forms. Well differentiated follicular carcinoma may grossly and microscopically resemble follicular adenoma. Diagnosis of malignancy in these cases is made when there is capsular and/ or vascular invasion.
- Distant spread is mainly by blood & metastases are common in lungs and bone.
- Usually poor prognosis.

3-Hurthle cell carcinoma: Characterized by malignant eosinophilic cells.

4-Anaplastic carcinoma: Composed of highly malignant spindle or giant cells.

5-Medullary carcinoma:

- Arises from parafollicular cells (C cells).
- Consists of malignant polyhedral cells separated by stroma containing amyloid.
- May be associated with paraneoplastic syndromes (carcinoid or Cushing syndrome)
- Prognosis is better than follicular carcinoma.

SPREAD OF THYROID CARCINOMA:

1-Direct to neck structures as recurrent laryngeal nerve producing hoarseness of voice, to larynx and trachea leading to stridor or asphyxia and to oesophagus producing dysphagia.

2-Lymphatic to cervical lymph nodes. It is the main route of spread of papillary carcinoma

3-Blood spread to bone, lung and brain :occurs relatively early in follicular carcinoma but rare or very late in papillary carcinoma

PROGNOSIS: Best with papillary carcinoma

CAUSES OF SOLITARY THYROID NODULE

- 1-Early nodular goiter (colloid nodule) (60%).
- 2-Adenoma (30%).
- 3-Carcinoma (5%).
- 4-Thyroiditis (Hashimoto's and subacute) (5%).

HYPOTHYROIDISM

CRETINISM (Infantile Hypothyroidism):

Aetiology:

- 1)Congenital thyroid hypoplasia (Sporadic Type).
- 2)Iodine deficiency during pregnancy (Endemic Type).

Manifestations: 1)Mental deficiency. 2)Dwarfism and hypogonadism. 3)Swollen lips and tongue.

MYXOEDEMA (Adult Hypothyroidism):

Aetiology:

- 1)Primary type (unknown cause, may be autoimmune).
- 2)Secondary due to thyroiditis, thyroidectomy, antithyroid drugs.

Manifestations: Low metabolic rate + accumulation of mucopolysaccharides in tissues. The effects are : 1) Increased body weight, swollen lips, tongue and skin (nonpitting oedema). 2)Hypercholesterolaemia.

THE PARATHYROID GLANDS

PRIMARY HYPERPARATHYROIDISM

(OSTEITIS FIBROSA CYSTICA or *Von Recklinghausen's Disease of Bone*)

AETIOLOGY: This is hyperfunction of parathyroids due to hyperplasia, adenoma or carcinoma.

PATHOLOGY:

- 1)Hypercalcaemia → metastatic calcification (see general pathology)..
- 2)Bone destruction leading to:
 - a)Fibrosis and cyst formation. Cysts are degenerative in nature and filled with hemorrhagic fluid.
 - b)Pathological fracture.
- 3)Brown tumor: This is a tumor-like swelling composed of collections of osteoclasts around areas of hemorrhage (haemosiderin).

SECONDARY HYPERPARATHYROIDISM

This is parathyroid hyperplasia excited by low serum calcium level in case of renal failure.

HYPOPARATHYROIDISM

Idiopathic or follow surgical removal of parathyroids (without replacement therapy). It leads to tetany.

PARATHYROID TUMORS

- These include 1)Parathyroid adenoma 2)Parathyroid carcinoma.
- They may function leading to primary hyperparathyroidism (see above).

THE PITUITARY GLAND

TUMORS

1-CRANIOPHARYNGIOMA:

A locally malignant tumor arising from remnants of Rathke's pouch in children.

Gross: A suprasellar noncapsulated solid or cystic mass with calcifications.

Microscopy:

Cystic spaces lined by stratified squamous epithelium and contain an oily fluid in which cholesterol crystals are present. The solid areas are composed of stroma and squamous epithelium with palisade arrangement of peripheral cells. Calcification is usually present.

Effects: Compression and destruction of:

- a-Pituitary causing hypopituitarism.
- b-Optic chiasma causing visual field defects.
- c-Third ventricle causing hydrocephalus.

2-PITUITARY ADENOMAS:

Old Classification of Pituitary Adenomas:

- **Acidophil adenoma** → growth hormone → gigantism or acromegaly.

- **Basophil adenoma** → Cushing's syndrome.
 - **Chromophobe adenoma** → pressure on the rest of pituitary → hypopituitarism.
- Recent Classification of Pituitary Adenomas:**
- **According to size:** a) Microadenoma (less than 1 cm) b) Macroadenoma (more than 1 cm)
 - **According to hormone secretion**
 - a) Prolactinoma
 - b) Growth hormone secreting adenoma
 - c) Adrenal corticotropinoma
 - d) Gonadotropinoma

PITUITARY HYPOFUNCTION

CAUSES:

- 1) **Idiopathic.**
- 2) **Primary tumors** compressing or destroying the pituitary as craniopharyngioma, chromophobe adenoma
- 3) **Secondary tumors (metastases)** destroying the pituitary.
- 4) **Tuberculoma** or sarcoidosis destroying the pituitary.
- 5) **Pituitary necrosis** which may be:
 - a) Ischemic necrosis (e.g. following post-partum hemorrhage)
 - b) Toxic necrosis (e.g. in cases of diphtheria).

EFFECTS: Hypofunction of anterior pituitary may result in one of the following syndromes:

- 1- **IN INFANTS (Pituitary Infantilism):** Decrease growth hormone → Dwarfism and hypogonadism.
- 2- **AT PUBERTY (Frolich's syndrome):** Obesity and hypogonadism.
- 3- **IN ADULTS (Simmond's Disease):** Loss of weight, amenorrhea & sterility.

DIABETES INSIPIDUS

- **Definition:** This is hypofunction of posterior pituitary
- **Aetiology:** 1) Idiopathic 2) injury of posterior pituitary by pituitary tumors or metastases 3) inflammation as in cases of encephalitis 4) injury associated with fracture base of skull.
- **Effects** are mainly polyuria (up to 10 liters per day) due to decrease of ADH

THE ADRENAL GLAND

TUMORS

TUMORS OF ADRENAL CORTEX:

- 1) **Epithelial:**
 - a) Benign: **Adenoma:** A capsulated yellowish growth occurring in young persons.
 - b) Malignant: **Carcinoma.**
- 2) **Mesenchymal:**
 - a) Benign: as fibroma, lipoma, neurofibroma and hemangioma.
 - b) Malignant: **Sarcomas.**
- 3) **Metastatic tumors.**

TUMORS OF ADRENAL MEDULLA:

1) **Neuroblastoma.**

Definition: A malignant embryonic tumor which affects children, usually under the age of 4 years.

Grossly the tumor appears as a large soft mass with areas of hemorrhage and necrosis.

Microscopically it consists of small round cells with dark nuclei (neuroblasts) sometimes arranged in a rosette pattern.

Spread:

- a) Direct to kidney and paravertebral structures.

- b) lymphatic to regional lymph nodes
- c) Blood spread → bone metastases particularly skull & orbit (Hutchinson's type) & liver metastases (Pepper's type).

2- **Ganglioneuroma**

It is a rare benign tumor composed of mature ganglion cells and neurofibrils.

3- **Ganglioneuroblastoma:** It consists of a mixture of the above two types.

4- **Paragangliomas & Pheochromocytoma:**

- Paragangliomas are tumors that arise from special secretory neuroepithelial cells. They may be adrenal or extra-adrenal. They are mostly benign, but may be malignant.
- **Pheochromocytoma** is an example of paragangliomas. It grossly appears as a capsulated brownish tumor. Microscopically it consists of large polygonal cells rich in chromaffin granules. The tumor secretes catecholamines leading to hypertension.

5- **Metastatic Tumors.**

ADRENOCORTICAL HYPERFUNCTION

Causes: Hyperplasia, adenoma or carcinoma of the adrenal cortex.

Effects:

- 1) **Aldosterone hypersecretion (Conn's Syndrome)** → hypertension, hyponatremia and hypokalemia.
- 2) **Hypersecretion of glucocorticoids (Cushing's Syndrome)** →
 - a) Increased gluconeogenesis → hyperglycemia & DM.
 - b) Destruction of tissue proteins → muscle weakness, osteoporosis & skin atrophy
 - c) Hypertension
 - d) Obesity (central type) characterized by moon face and buffalo hump
 - e) Decreased blood lymphocytes (lymphocytopenia) & lowered immunity
- 3) **Hypersecretion of androgens (Adrenogenital Syndrome)** leads to:
 - a) In boys: → Precocious puberty
 - b) In girls: → increased pubic and face hair. Delayed onset of menstruation.
 - c) In females: Defeminization (virilism): enlarged clitoris, hirsutism & deepening of voice.

ADRENOCORTICAL HYPOFUNCTION

ACUTE ADRENAL INSUFFICIENCY:

Causes:

- 1) Septicemia as in meningococcal meningitis
- 2) Sudden withdrawal from prolonged corticosteroid therapy
- 3) Bilateral Adrenalectomy (if no adequate replacement therapy is given)
- 4) Acute adrenal hemorrhage as in hemorrhagic blood diseases

Effects: A fatal condition due to severe hypotension & shock.

CHRONIC ADRENAL INSUFFICIENCY (ADDISON'S DISEASE):

Aetiology: Chronic bilateral adrenal gland destruction due to:

- 1) Autoimmunity.
- 2) Amyloidosis.
- 3) Tuberculosis.
- 4) Metastases.

Effects:

- 1) Low aldosterone level → loss of sodium & water → hypotension, dehydration & potassium retention.
- 2) Low glucocorticoid level → hypoglycemia.
- 3) Low androgen level → muscle atrophy.
- 4) Rise of ACTH (by feed-back mechanism) → melanocyte stimulating action → skin pigmentation

THE PANCREAS

DIABETES MELLITUS

DEFINITION:

Diabetes mellitus (DM) is a systemic disease resulting from deficient insulin secretion or development of resistance to insulin. This leads to disturbance of carbohydrate metabolism and secondary disturbance of fat metabolism, reflected on all body systems.

AETIOLOGY (TYPES) OF DIABETES MELLITUS:

A) SECONDARY DM: This is a rare type caused by:

- 1- Destruction of islets of Langerhans by:
 - a- Pancreatitis
 - b- Pancreatic tumors
 - c- Hemochromatosis.
- 2- Endocrine disease as Cushing's syndrome.

B) PRIMARY DM: A very common disease. Two major subtypes; type I (10%) and type II (90%).

1- Type I: Insulin-dependent diabetes mellitus (IDDM):

- It was formerly called juvenile onset or ketosis-prone diabetes mellitus.
- It affects children & young adults.
- Pathogenesis is still unclear. Suspected factors include:
 - a) Autoimmunity as evidenced by:
 - Early infiltration of the islets by T cells of both CD4+ and CD8+ types (insulinitis)
 - Islet cell antibodies were also found in 90% of patients early in the disease course.
 - b) Genetic susceptibility: Important factor, but the mode of inheritance is unknown.
 - c) Environmental factors such as viral infections (mumps, measles, coxsackie B virus, infectious mononucleosis) may participate, but alone cannot cause type I diabetes.

2- Type II: Non-insulin dependent diabetes mellitus (NIDDM):

- It was formerly called adult onset diabetes mellitus.
- It affects adults, usually above the age of 30 years.
- There are 2 subtypes:
 - a) The obese type (80%).
 - b) The non obese type (20%).
- Pathogenesis is not clear. An unrecognized genetic factor is involved leading to one or more of:
 - a) Synthesis of abnormal insulin molecules
 - b) Impaired response to insulin (resistance)
 - c) Impaired release of insulin.

PATHOLOGY OF THE PANCREAS IN DM:

Gross picture:

- 1) In **secondary DM** it shows the gross features of the causative disease (tumor, hemochromatosis ... etc)
- 2) In **primary DM** the pancreas looks normal.

Microscopic picture:

- 1) **Secondary DM:** It shows the specific lesions leading to pancreatic destruction (e.g tumor, pancreatitis... etc)
- 2) **Primary DM:**
 - **Type I DM:** There is
 - a) Reduction in the number and size of islets of Langerhans
 - b) Beta cell degranulation and depletion.
 - c) Lymphocytic infiltrates (insulinitis).
 - **Type II DM:**
 - a) There is no insulinitis.
 - b) Mild atrophy of beta cells.
 - c) Amyloid replacement of the islets may occur in long standing type II cases.

EFFECTS & COMPLICATIONS OF DM:

1- Metabolic Disturbances:

- a) **Hyperglycemia** and glucosuria.
- b) **Osmotic diuresis** (polyuria) → profound loss of water and electrolytes (Na, K and Mg).
- c) **Ketoacidosis** (in type I DM). This leads to **ketotic coma**.
- d) **Nonketotic hyperosmolar coma**: It occurs in type II DM; particularly the elderly. It is due to severe dehydration from sustained hyperglycemic diuresis.
- e) **Hyperlipaemia**.
- f) **Loss of weight**.

2- Cardiovascular Lesions:

- a) **Microangiopathy**: This is thickening of capillary basement membranes → serious effects as:
 - Lowered immunity due to defective exudation in response to infection.
 - Neuropathy.
 - Nephropathy: The affected glomerular capillaries leak plasma proteins → nephrotic syndrome

b) **Hyaline Arteriosclerosis**: Hyalinosis of walls of arterioles

c) **Atherosclerosis** and superimposed thrombotic lesions. Manifestations include:

- Angina pectoris.
- Myocardial infarction.
- Cerebral ischemia.
- Diabetic gangrene.
- Renal ischemia...

3- Renal lesions: Diabetic Nephropathy:

- a) **Interstitial nephritis/ pyelonephritis** due to infection
- b) **Hyaline arteriosclerosis** of afferent and efferent arterioles.
- c) **Diffuse or nodular glomerulosclerosis**: Diffuse or nodular thickening of basement membranes of glomerular capillaries (due to microangiopathy) resulting in nephrotic syndrome. The nodular type is known as Kimmelsteil-Wilson disease
- d) **Atherosclerosis of renal artery**.
- e) **Vacuolization of tubules** due to glycogen accumulation
- f) **Renal failure**.

4- Retinopathy: Two subtypes:

- a) **Nonproliferative retinopathy**: Retina shows hemorrhage, edema, microangiopathy & microaneurysms.
- b) **Proliferative retinopathy**: Retina shows neovascularization and fibrosis. Retinal hemorrhage may occur due to rupture of the new capillaries or from microaneurysms. It is serious & may → blindness.

5- Nervous system:

- a) **Peripheral neuropathy**: It symmetrically affects both lower extremities. Both motor and sensory functions are affected.
- b) **Cerebral ischemia and infarcts**.

6- Infections of skin and other organs due to lowered immunity and tissue hyperglycemia.

7- Others such as trophic skin ulcers (mainly big toe), hepatic steatosis & impotence.

PANCREATIC TUMORS

See before (page 110)

DISEASES OF THE NERVOUS SYSTEM

INFLAMMATORY DISEASES

MENINGITIS

Inflammation of the meninges covering the brain & spinal cord, may rarely affect the dura (pachymeningitis), but more commonly affects pia-arachnoid (leptomeningitis). Types include:

1-Septic (suppurative) Meningitis.

2- Nonsuppurative:

- Tuberculosis.
- Viral.
- Fungal.
- Syphilis.

SEPTIC MENINGITIS

AETIOLOGY:

1-Meningococcal meningitis:

- Meningococci are transmitted by droplet infection (mainly children).
- The organism cause nasopharyngitis followed by septicemia & affection of meninges by blood spread.

2-Other pyogenic bacteria: as Staphylococci, Pneumococci reaching the meninges by blood spread from lung infections, otitis media...etc.

PATHOLOGY (of meningococcal meningitis):

Gross:

- The pia and arachnoid membranes are thick, congested and covered with purulent exudate.
- The ventricles are dilated and together with the subarachnoid space contain turbid cerebrospinal fluid.
- The choroid plexus is congested.

Microscopy: The affected meninges show dilated capillaries, several polymorphs, pus cells and macrophages as well as excess fibrin

CSF: If CSF is withdrawn for analysis:

- It comes out with increased tension
- Contains many neutrophils & pus cells
- High protein content
- Low sugar.
- Culture will show the causative organisms.

COMPLICATIONS:

- Arterial thrombosis leading to cerebral infarction.
- Thrombophlebitis producing pyemia.
- Adrenal hemorrhage and acute adrenal insufficiency due to septicemia.
- Fibrosis (if the patient survives) resulting in a)Hydrocephalus. b)Cranial nerve paralysis.

CEREBRAL ABSCESS

AETIOLOGY:

Bacteria: Large variety of pyogenic bacteria as staphylococci, pneumococci, E coli & streptococci. Mixed infection with more than one organism may occur.

Routes of infection: Cerebral abscess occur as a complications of other diseases:

1-Direct spread: a)Chronic suppurative infection of middle ear, mastoid air spaces and paranasal sinuses may be associated with erosion of the thin bony plates producing temporal lobe, cerebellar and frontal lobe abscesses respectively. b)Infection following a skull fracture.

2-Blood spread a)from suppurative lung diseases as lung abscess, bronchiectasis & empyema b)Pyemic abscesses may develop due to septic emboli e.g derived from acute infective endocarditis. These abscesses are multiple and small.

PATHOLOGY:

1-Site is variable according to route of infection (see above).

2-Gross: The abscess appears as a swelling having liquefied center filled with pus. The surrounding brain shows oedema. If the abscess is not treated it becomes surrounded by a fibroglial wall (chronic abscess)

3-Microscopy: The abscess contains liquified necrotic tissue, neutrophils & pus cells. The wall of the abscess shows congested capillaries and acute inflammatory cells as well as fibroglia in chronic cases.

COMPLICATIONS:

- Increased intracranial pressure.
- Rupture into the ventricular system.
- Spread of infection (meningitis, sinus thrombophlebitis).

ENCEPHALITIS

This is diffuse inflammation of the brain. It is more common in AIDS. It may be caused by:

- Virus (as herpes, rabies, poliomyelitis & others)
- Pyogenic bacteria
- Fungus as cryptococcosis & disseminated candidiasis
- Parasitic infection as malaria.

VIRAL INFECTIONS OF THE NERVOUS SYSTEM

1-POLIOMYELITIS

AETIOLOGY: It is a viral infection of the nervous system by poliovirus, an enterovirus transmitted by fecal-oral route. The virus enters the body through the intestine and multiplies in lymphoid tissues of oropharynx and intestine (incubation period), then invade the blood stream (viremia) to reach the brain and spinal cord. Poliomyelitis is now rare because of routine immunization during childhood.

PATHOLOGICAL FEATURES: Poliovirus selectively infects meninges & lower motor neurons:

1-Meninges → acute lymphocytic meningitis.

2-Lower motor neurons in the anterior horn of the spinal cord & medulla oblongata are affected:

- Inflammation characterized by perivascular lymphocytes and plasma cells.
- Motor nerve cells show intranuclear inclusion bodies & nerve cell destruction followed by gliosis.
- Motor nerve: Nerve cell destruction is followed by demyelination of the corresponding peripheral nerve → paralysis of affected muscles → muscle atrophy.
- The atrophic muscles undergo fibrous contracture.
- Mortality from poliomyelitis occurs in the acute phase due to paralysis of respiratory muscles.

2-RABIES

AETIOLOGY: This rare viral disease is transmitted to man by bites of infected animals (commonly dogs).

PATHOLOGICAL FEATURES: The virus invades the nerve cells of the brain stem & posterior horns of spinal cord causing intracytoplasmic inclusion bodies (Negri bodies), nerve cell damage and inflammation characterized by perivascular lymphocytes & plasma cells.

CLINICAL: Spasm of pharyngeal muscles (difficult swallowing), convulsions, coma & death.

3-HERPES ZOSTER

AETIOLOGY: Adult infection with Varicella zoster virus. If the same virus is transmitted to children will cause a different disease (chicken pox).

PATHOLOGY:

- 1-Inflammation & degeneration of the spinal posterior root ganglia. It may also affect the cranial Nerves, spinal cord or brain.
- 2-It is mainly manifested by multiple painful skin vesicles on face & trunk. The vesicles dry during three weeks..

VASCULAR DISEASES OF NERVOUS SYSTEM

INTRACRANIAL HAEMORRHAGE

Depending on the anatomical site of hemorrhage, it is divided into meningeal hemorrhage and intracerebral hemorrhage

A- MENINGEAL HAEMORRHAGE:

- 1- **Extradural hemorrhage:** (Epidural hematoma): Due to traumatic injury of middle meningeal artery. The blood collected rapidly leading to compression of brain, increased intracranial pressure and herniation.
- 2- **Subdural hemorrhage:** Due to traumatic injury of veins crossing the subdural space. The venous blood accumulates slowly with organization later on.
- 3- **Subarachnoid hemorrhage:** Due to:
 - a) Rupture of aneurysm of cerebral artery.
 - b) Extension from underlying cerebral hemorrhage.
 - c) Hemorrhagic blood diseases as leukemia, purpura...etc.

B- CEREBRAL HAEMORRHAGE:

- 1- **Massive cerebral hemorrhage (Stroke):** Rapidly fatal.

Causes:

- a) Hypertension: 80% of cases.
- b) Traumatic.
- c) Hemorrhage inside tumors.
- d) Ruptured cerebral aneurysm.
- e) Hemorrhagic blood diseases as purpura, leukemia,...

Pathology: Massive extravasation of blood usually within the cerebral hemispheres, may be extension to ventricles or subarachnoid space, associated with compression of adjacent parenchyma.

- 2- **Punctate or petechial hemorrhage:** Small hemorrhagic spots are due to:
 - a) Infections as encephalitis.
 - b) Trauma.
 - c) Severe anoxia.
 - d) Hemorrhagic blood diseases.

CEREBRAL ANEURYSMS

TYPES:

- 1- **Congenital (berry) aneurysms:** These are multiple small pin-head sized arterial dilatation at the bifurcation of cerebral vessels in the circle of Willis. They are due to congenital absence of media.
- 2- **Mycotic aneurysms:** Secondary to inflammatory weakness in the vascular wall in the circle of Willis. They are secondary to complication of subacute infective endocarditis and polyarteritis nodosa.
- 3- **Atherosclerotic aneurysms:** Common sites are the basilar and middle cerebral arteries.
- 4- **Arterio-Venous aneurysm:** Communication between the internal carotid artery and the cavernous sinus secondary to trauma.

COMPLICATIONS:

- 1- Subarachnoid hemorrhage due to rupture.
- 2- Thrombosis and calcification.
- 3- Pressure on surrounding structures.

CEREBRAL INFARCTION

See general pathology.

HYDROCEPHALUS

DEFINITION: This is a chronic accumulation of CSF inside the ventricular system leading to its dilatation and consequently atrophy of the brain tissue.

AETIOLOGY:

- 1- **Increased CSF production** due to choroid plexus papilloma.
- 2- **Obstruction of CSF flow** due to:

a) **Congenital causes (non-communicating type of obstructive hydrocephalus):** Due to congenital narrowing of ventricular foramina or aqueduct

b) **Acquired causes:**

- Meningitis → fibrosis → obstruction of subarachnoid space.
- Brain tumor or brain abscess
- Subtentorial masses → upward compression of brain → obstruction of subarachnoid space

- 3- **Decreased CSF absorption** due to:

a) **Congenital causes:** Congenital aplasia of arachnoid villi.

b) **Acquired causes:**

- Damage of arachnoid villi in case of meningitis.
- Thrombosis of superior sagittal sinus.

TYPES:

1- **Communicating type:**

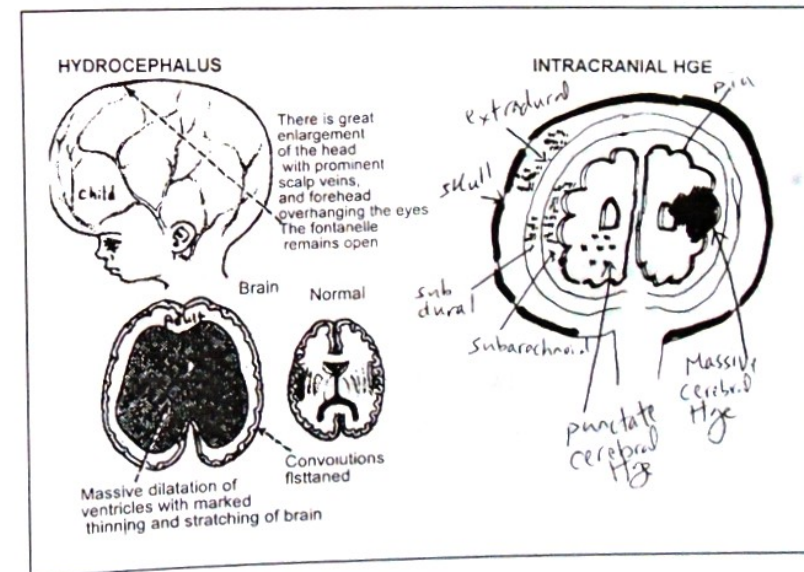
- a) Obstructive (obstruction at the level of subarachnoid space)
- b) Non-obstructive due to excess CSF production or decreased CSF absorption.

2- **Non-communicating:** It is an obstructive type. Obstruction is within the ventricles.

PATHOLOGY: There is ventricular dilatation with excess CSF:

1- **In infants,** hydrocephalus leads to enlargement of the head due to separation of skull sutures.

2- **In adults,** hydrocephalus leads to increased intracranial tension which may → brain herniation → death.



TUMORS OF THE NERVOUS SYSTEM

EFFECTS OF INTRACRANIAL TUMORS:

- 1- Increased intracranial tension leading to headache, vomiting, blurred vision, tremors, brain herniation.
- 2- Local effects depending on tumor location e.g paralysis

CLASSIFICATION:

• According to site:

- 1-Supratentorial
- 2-Infratentorial

• According to cell of origin:

1-Metastatic tumors.

2-Primary tumors

a) Gliomas (tumors of neuroglia)

- Astrocytoma
- Oligodendroglioma
- Ependymoma & choroid plexus papilloma
- Glioblastoma multiforme.

b) Neuronal tumors:

- Neuroblastoma
- Ganglioneuroma
- Ganglioneuroblastoma

c) Primitive undifferentiated tumors: Medulloblastoma

d) Pineal body tumors:

- Pineoblastoma
- Pineocytoma

e) Meningeal tumors:

- Meningioma
- Malignant meningiomas
- Meningeal hemangiopericytoma

f) Lymphoma May be secondary or primary, the later is mostly high grade B cell lymphoma. Common in AIDS & immunosuppressive states)

g) Vascular tumors:

Hemangioma, hemangioblastoma, angiosarcoma, hemangiopericytoma...

h) Developmental tumors:

- Teratoma /dermoid cyst
- Craniopharyngioma.

i) Peripheral nerve sheath tumors:

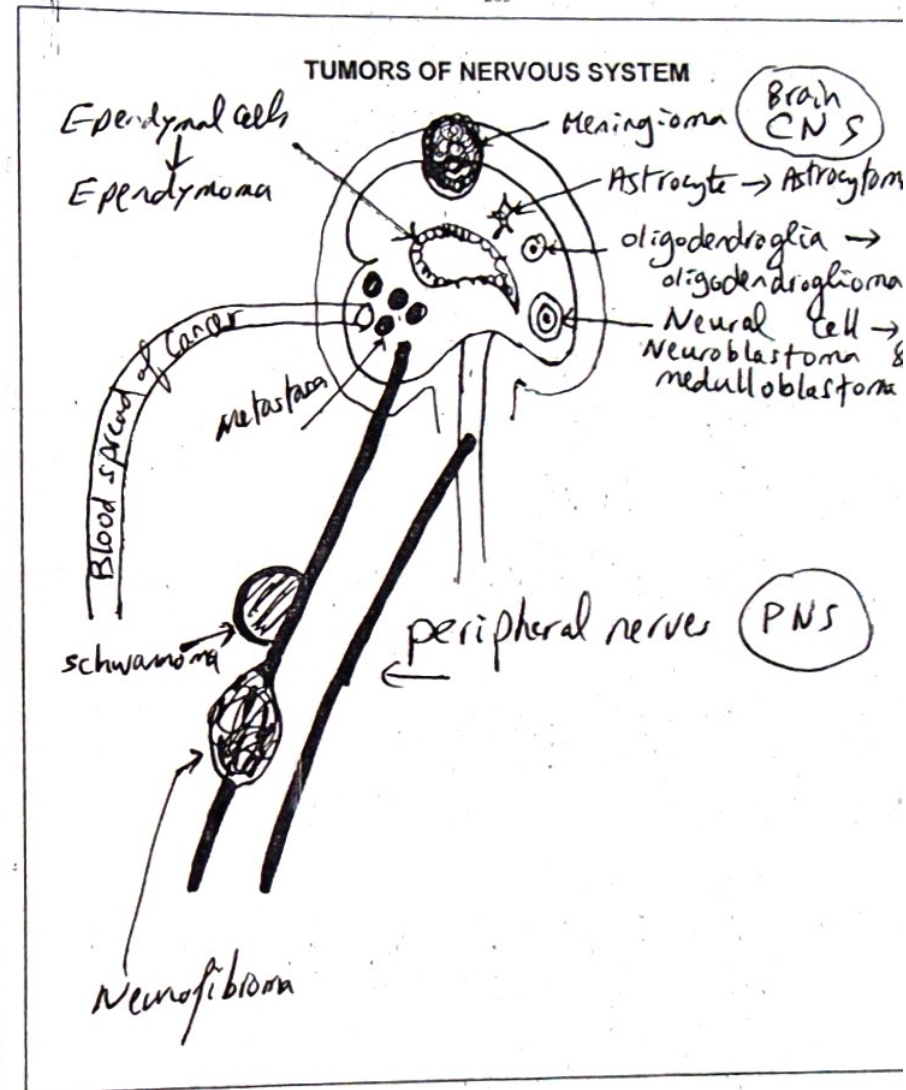
- Schwannoma
- Neurofibroma,
- Neurofibromatosis
- Malignant schwannoma

- According to WHO (World Health Organization) Grading System: This depends on many factors including rate of growth, clinical behavior, tumor cellularity, tumor vascular pattern & tumor necrosis. All primary tumors of CNS can be graded as WHO grade I, II, III or IV.

METASTATIC TUMORS

They may be derived from:

- 1-Carcinomas (e.g bronchogenic, renal & mammary carcinoma)
- 2-Sarcomas
- 3-Other malignancies:
 - a) melanoma
 - b) lymphoma & leukemia.



GLIOMAS

A) ASTROCYTOMA: Most common primary tumor of CNS. Several types

1-Piloctic Astrocytoma (WHO Grade I): This is the only astrocytic tumor with good news (considered benign). It usually affects children. It mainly occurs in the cerebellum.

Gross: It appears as a circumscribed cystic mass with a solid mural nodule.

Microscopically it consists of bipolar astrocytes.

2-Low Grade Astrocytoma (WHO Grade II) (also called Diffuse astrocytoma):

The tumor is more common in adults and usually affects the cerebral hemispheres.

Gross: It appears as an ill-defined infiltrative whitish growth.

Microscopically it shows moderate cellularity with moderate cellular atypia. The cells are either fibrillary astrocytes (more common) or protoplasmic astrocytes.

3-Anaplastic Astrocytoma (WHO Grade III):

It usually affects the cerebral hemispheres of adults.

Grossly appears as an infiltrative growth.

Microscopically: A highly cellular growth composed of pleomorphic astrocytes with mitotic activity, but no necrosis.

Gemistocytic astrocytoma: It is a variant of high grade astrocytoma (grade III, rarely grade II).

Microscopically it consists of large astrocytes with abundant pink cytoplasm (gemistocytes) & atypical nuclei showing mitoses.

4-Glioblastoma multiforme (WHO Grade IV):

A highly malignant tumor. More common in adults.

Cerebral hemispheres is the most frequent site.

Grossly appears as an infiltrative growth, usually large-sized, showing hemorrhage, necrosis & cysts.

Microscopically it shows high cellularity with marked cell anaplasia, cell necrosis and vascular endothelial proliferation. It is the most malignant primary brain tumor.

B) OLIGODENDROGLIOMA

A rare tumor occurring in cerebral hemisphere in adults. The tumor is usually a WHO grade II slowly growing neoplasm. It is rarely grade I or III. Grade IV tumor is a glioblastoma multiforme.

Gross: A circumscribed solid or gelatinous tumor, commonly showing calcifications visible on X-ray.

Microscopy: Small uniform cells having rounded lymphocyte-like nuclei and pale staining to clear cytoplasm.

C) EPENDYMOMA

It is uncommon neoplasm, occurring in all ages, arising from ependymal cells lining the ventricles or spinal canal. About 60% of cases occur in fourth ventricle. It is commonly WHO grade I neoplasm (but may be grade II, III or IV). Higher grade tumors have the ability to spread via the cerebrospinal fluid.

Gross: A circumscribed reddish brown fleshy mass arising in relation to the ventricular system.

Microscopy: A cellular growth composed of small polygonal cells arranged around vessels (perivascular) forming pseudorosettes, or around empty spaces forming true rosettes. Sometimes it forms papillary projection composed of connective tissue cores covered by hyperplastic ependymal cells. Rare variants of ependymoma include myxopapillary ependymoma and choroid plexus papilloma.

Myxopapillary ependymoma:

A specific type occurs in the filum terminale and presents as a cauda equina tumor in young adults.

Choroid plexus papilloma:

A rare tumor occurring in the ventricles of young children. May lead to excess CSF secretion → hydrocephalus.

MEDULLOBLASTOMA

It is a highly malignant (WHO grade IV) rapidly growing tumor that exclusively occurs in the cerebellum of children or less commonly adults. The tumor arises at the middle line, but may rarely occur in one of the cerebellar hemispheres.

Gross: A greyish white fleshy mass with areas of necrosis and hemorrhage & infiltrative margins. It may project in the 4th ventricle causing obstruction to CSF flow → hydrocephalus.

Microscopically, the tumor consists of small oval cells with dark nuclei and little cytoplasm. The cells may be arranged around blood vessels giving a pseudorosette pattern. Mitotic figures are frequent.

MENINGEAL TUMORS

A) MENINGIOMA:

It is a relatively common tumor arising from dura or leptomeninges. Most examples occur in adults. Females are more commonly affected. Most cases are benign, but some tumors are malignant.

GROSS: Most types of meningioma form a globular capsulated firm greyish mass. The cut surface may show whorly appearance and calcific foci. The tumor may compress the brain or spinal cord.

MICROSCOPY: There are several types of meningioma:

1) Meningotheliomatous (syncytial) type: The tumor consists of concentric whorls of proliferated meningeothelial cells (oval cells with indistinct cell borders, pale cytoplasm & regular round nuclei). Cell whorls are separated by fibrovascular stroma.

2) Psammomatous type: It is a meningotheliomatous type in which some of the cell whorls show central hyalinosis and calcification. These central calcific spherules are called psammoma bodies.

3) The fibroblastic type: It resembles fibroma.

4) The transitional type: A mixture of meningotheliomatous (or psammomatous) & fibroblastic types.

5) Uncommon types: e.g. inflammatory meningioma, secretory meningioma, clear cell meningioma and papillary (aggressive) meningioma.

B) MALIGNANT MENINGIOMA: These are infiltrative growths, composed of proliferated meningeothelial cells showing mitotic activity & necrosis.

C) HEMANGIOPERICYTOMA

PERIPHERAL NERVE SHEATH TUMORS

They arise from peripheral nerves (cranial or spinal nerves) including the nerve roots.

A) SCHWANNOMA (NEURILEMMOMA)

A benign tumor arising from Schwann (neurilemma) cells of the peripheral (cranial or spinal) nerves.

Gross: A firm greyish capsulated mass at one side of the nerve. The 8th cranial (acoustic) nerve is one of the famous sites of schwannoma. A tumor in this site (cerebellopontine angle) leads to compression of midbrain and cerebellum.

Microscopy: The proliferating Schwann cells assume one or both of two patterns:

a) Antoni type A: The cells are spindle-shaped with elongated nuclei. The cells occur in parallel bundles; thus the nuclei show a palisade pattern.

b) Antoni type B: The cells are larger, ovoid and haphazardly arranged. The stroma shows microcystic and myxomatous changes.

B) NEUROFIBROMA

Grossly appears as a rubbery expansion of the affected nerve, not demarcated from the nerve.

Microscopically, composed of fibrous tissue intermingled with Schwann cells and nerve fibrils. Neurofibroma has a significant risk of malignant transformation

C) NEUROFIBROMATOSIS (Von Recklinghausen's disease of nerves)

It is a familial disease (autosomal dominant inheritance) of two types:

Type I (NF1): is characterized by:

- Multiple neurofibromas; mainly cutaneous. Malignant transformation is not uncommon.
- Acoustic Schwannomas.
- Cafe au lait spots (hyperpigmented skin macules).
- Eye lesions: a) Optic nerve gliomas. b) Pigmented nodules of iris.

Type II (NF2): It resembles type I without eye affection.

d) MALIGNANT SCHWANNOMA:

Occurs de novo or complicates pre-existing Von Recklinghausen's disease.

PERIPHERAL NEURITIS

DEFINITION: This is inflammation and degeneration of peripheral nerves.

CAUSES:

1-Diabetes mellitus: It is one of the most common causes of peripheral neuritis.

2-Chronic alcoholism.

3-Chronic lead poisoning.

4-Beriberi.

5-Leprosy.

6-Toxaemia as diphtheria.

7-Acute post-infective polyneuritis : It follows some infective diseases as measles and influenza or after vaccination and is thought to be of allergic nature.

8-Ischaemia as in cases of polyarteritis nodosa.

9-Infections as measles.

10-Traumatic as in case of disc prolapse.

CEREBRAL OEDEMA

a- Vasogenic due to increased vascular permeability as with cerebrovascular accidents, trauma, tumors and infections. The brain is heavy, swollen and soft. There is tissue vacuolation involve mainly white matter.

b-Cytotoxic: Secondary to altered cell regulation of fluid, seen in anoxia or toxic/metabolic disturbances. The fluid is intracellular and tends to involve the gray matter.

c-Interstitial: Transudation of fluid from the ventricular system across the ependymal lining (characteristic of increased intraventricular pressure).

BRAIN HERNIATION

It is bulging of part of brain through openings of the dural partitions of the cranial cavity or across openings of the skull due to rise in intracranial pressure. The major herniations are:

a- Subfalcine: cingulate gyrus herniates under the falx.

b-Transtentorial : medial temporal lobe (uncus) passes over the free edge of the tentorium leading to distortion of the adjacent mid brain/pons and tearing of feeding vessels producing fatal hemorrhage.

c-Tonsillar: cerebellar tonsils herniate through the foramen magnum which may compress the medullary centers.

DEMENTIAS

Alzheimer's disease: It is due to senile atrophy of brain, mainly frontal lobes.

Pick's disease: Also occurs in old ages. Characterized by frontal and temporal lobe atrophy. May be familial (autosomal dominant)

Multi-infarct dementia

Creutzfeldt-Jacob Disease

DEMYELINATING DISEASES

A group of diseases characterized by idiopathic loss of myelin with relative preservation of axons. Best example is multiple sclerosis.

SYSTEMIC PATHOLOGY

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Other Books By The Author

- *General Pathology
- *Simplified Basic General Pathology
- *Coloured Atlas Of Gross Pathology
- *Coloured Atlas Of Histopathology
- * Pathology Questions(in Press)

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